DISEASES OF THE SKIN

BY

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PREFACE

I HAVE tried in this book to provide a text that undergraduates and general practitioners may use for reference and that will serve as introductory reading for postgraduate students.

The basic scope of dermatological practice is much the same all over the world, and if I stress some conditions commoner in Southern Africa than elsewhere I do not think the balance has been affected thereby.

The art of recognition of the lesions and patterns of evolution in skin diseases can be learnt only by the observation of many cases, and I have not attempted to reduce it to writing.

The importance of histopathological examination in the investigation of skin disorders cannot be overestimated, and I have given detail enough to indicate the nature of the processes involved. Postgraduate students will need to supplement their studies in this, as in other subdivisions of the subject, in more specialized works. A bibliography of main references for further comparative and specialized reading is appended.

To avoid repetition, a list of prescriptions for topical applications and general instructions for the use of such remedies as corticosteroid hormones, antihistaminics, antimalarials and antibiotics are included in Chapter IV, and instructions for the use of the antifungous antibiotics will be found in the introduction to Chapter XVI.

The system of classification is largely orthodox, but I have occasionally considered some conditions out of context, e.g. epidermolysis bullosa next to porphyria, in order to stress a relationship. The nomenclature adopted is usually that which is at present most commonly used in the literature, but when common usage infringes on priority, as in some of the syndromes, the fact is stated.

I. M.

Cape Town, 1960

ACKNOWLEDGEMENTS

A NUMBER of colleagues and institutions in Africa, Europe and the Americas have generously contributed photographs to fill the gaps in my collection. When an illustration has been borrowed its provenance is noted under the title, but I must also thank certain people who are not individually cited in this way

Among these are Professor A. J Brink, Dr R. L. M Kotzé and my colleagues at Karl Bremer Hospital and the University of Stellenbosch Professor H W Synman, Dr G H Findlay and Dr I K. Venter at the University of Pretoria Dr R. Lang and his colleagues in the Department of Dermatology at the University of Cape Town Mrs M. E. Pfeiffer who lent the photographs from the collection of her late husband, Dr D H Pfeiffer who was Medical Officer of Health in Bloemfontein Dr Hugh Wallace of St. Thomas's Hospital, London Dr A. Touraine, Editor of the *Annales de Dermatologie et de Syphiligraphie* Dr F W F Purcell who lent from his own collection and from that of the late Dr D C. McArthur and Dr A. P Blignault, Editor of the South African Medical Journal, in which some of the illustrations have already appeared. The photographs lent by Drs. A. G Shaper and P W Hutton come from the collection of the Makerere College Medical School, Kampala, Uganda. Drs. J M. Martin, W J Pepler and H. I Lurie collaborated with me in the investigation of some of the cases illustrated.

Some of the illustrations have already appeared in my earlier books, and I would like again to thank the lenders who were the following The Curator of the Museum of the London Hospital Medical College the Medical Committee of St. John's Hospital for Diseases of the Skin, London the Director of the Wellcome Museum of Medical Science, London and Drs. Sydney Thomson, J E. Schneider G Leslie, S. R. A. Beckett and L. B Bourne. Mr Norman K Harrison took the original photographs used in these books.

Many of the photographs from my own collection were taken by Mr Robert Ellis, A.I B P A.C.P I P., Department of Clinical Photography at Karl Bremer Hospital, some by his

predecessor Mr P de Chavigny and others by Mr The Marais, Department of Clinical Photography Pretoria Gener Hospital

Only main subject references have been included in th bibliography and I hope that those of my colleagues wh recognize that I have quoted from their articles will accep this acknowledgement of my indebtedness

I must, finally thank Mrs F J F Kellerman who typed th manuscript, my wife who read the proofs and my publisher Mr Charles Macmillan of E & S Livingstone Ltd for advic and instruction

CONTENTS

CHAPTER I

ANATOMY AND PHYSIOLOGY

ANATOMY

THE skin is a dynamic organ composed of ectodermal and mesodermal components. The outer covering of epidermis (epithelium) is of ectodermal origin and lies upon the dermis or corium beneath the dermis is the hypoderm or subcutaneous tissue Both dermis and hypoderm arise from mesoderm

The embryonic epidermis originally consists of a single layer of cells which, during the second intrauterine month, differentiates into two to form an outer *periderm* or *epitrichium* and an inner layer *the stratum germinativum in the third month, a third layer* the *stratum intermedium*, appears between them. At the fourth month, the periderm separates to help in the formation of the *vernix caseosa* and the cells of the stratum intermedium multiply to develop into the *stratum Malpighii*

From the stratum germinativum develop the basal cells of the adult epidermis, eccrine sweat gland germ cells and primary epithelial germ cells from which arise hairs and sebaceous and apocrine glands.

Melanocytes appear in the epidermis about the third month. The balance of opinion is now in favour of their origin in the neural crest and subsequent migration with the nerves to the epidermis. They are still however believed by some authors to be, simply modified basal cells.

The foetal dermis consists at first of closely packed spindle-shaped mesodermal cells. In the third month, these cells develop into fibroblasts and reticulum fibres and later collagen fibres can be identified. Fat also develops in the third month, but elastin is seen only at the sixth month Collagen and elastic fibres are probably precipitated out of the intercellular ground substance by some enzyme of mesodermal cells.

In the mesoderm develop the blood vessels and primitive

blood cells or haemocytoblasts, the bones and cartilages Multipotent mesodermal cells remain in the adult dermis and other organs and may if a suitable stimulus arises, take up again their primitive functions this is the basis of the lesions of the diseases of the reticulo-endothelial and haemopoietic systems.

THE EPIDERMIS

In sections of normal skin it is seen that the dermo-epidermal junction is a wavy line This is due to the fact that

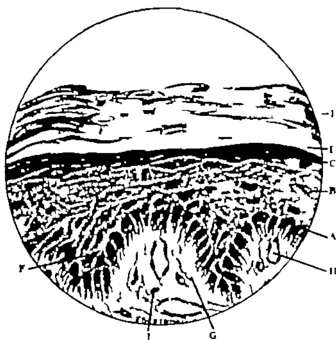


FIG. 1

Normal skin. A: stratum basale B stratum Malpighii C: stratum granulosum D stratum lucidum E stratum corneum F rete peg; G: dermal papilla H capillary J connective tissue cell.

(*Henry Haber* The Eczemas

the under surface of the epidermis is studded with innumerable blunt digitate projections known as rete pegs the corresponding upward projections of the dermis are known as dermal papillae

In the adult epidermis four distinct layers of cells can be distinguished except in the palms and soles where a fifth layer is seen. The skin is not an inert structure and the various

epidermal layers represent a process of gradual maturation or evolution of the cells in the deepest layer and their upward growth until they are shed in an invisible desquamation. Mitotic figures are seen in the cells of the stratum basale and stratum Malpighii (Figs. 1 and 2)

The stratum basale stratum germinativum or basal layer lies against the dermis and contains nucleated cells of two different types, basal cells and melanocytes. Basal cells are columnar or cylindrical and lie with their long axis perpendi-

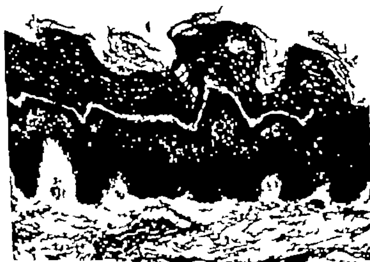


Fig.
Normal skin.

[Henry Haber]

cular to the dermo-epidermal line of junction. They are united by fine protoplasmic intercellular bridges to each other and to overlying cells. They may appear on routine staining to contain melanin granules, but special methods show that this is not so. Fine cytoplasmic processes from the basal cells interdigitate with reticulum fibres of the dermis, but a basement membrane is interposed.

In sections stained by routine methods some cells with clear cytoplasm and a small dark nucleus are seen between the

basal cells These are melanocytes (clear or dendritic cells) and stain with Bloch's dopa stain (they can form melanin) and silver stains (they contain melanin) Silver staining shows that they send out long dendritic processes containing melanin granules

The subepidermal basement membrane In some routinely stained skin sections a fine eosinophil membrane may be seen to separate the dermis from the epidermis. It appears from its special staining properties to consist of a mixture of a network of fibres (reticulin or degenerate collagen) and mucopolysaccharides To its under surface are attached very numerous delicate fibres arising from the dermal elastic plexus



Fig 3
Intercellular bridges.
M Rudin]

its upper surface is invaginated by cytoplasmic digitations from the cells of the stratum basale

The basement membrane completely divides the epidermis from the dermis while assuring their adherence, and it is lesions of the membrane which permit the formation of subepidermal bullae.

The stratum Malpighii (stratum mucosum, squamous or prickle-cell layer) lies above the stratum basale and consists of a mosaic of nucleated polygonal cells that become flattened in the upper layers Across the spaces between the cells run intercellular bridges (prickles) Lymphatic fluid can circulate between the cells Phase contrast and polarization microscopy have shown that tonofibrils (probably consisting of keratin) appear to run uninterruptedly across the cells and through

the intercellular bridges. Each intercellular bridge shows a small nodular thickening the nodule of Bizzozero (Fig 3)

The stratum granulosum or granular layer lies over the stratum Malpighii, is two or three cells thick, and consists of flattened nucleated cells whose cytoplasm is filled with coarse granules. The granules consist of *keratohyalin* which is probably identical with desoxyribonucleic acid. This layer and the stratum corneum are usually absent in the buccal mucosa.

The stratum lucidum is seen only in the palms and soles where it lies above the stratum granulosum. Its cells are not nucleated they are flat and transparent because an oily substance, *eleidin*, is contained within them Eleidin is believed to result from liquefaction of keratohyalin granules.

The stratum corneum or horn layer is the outermost layer of the epidermis and consists of closely packed, flattened cells full of keratin and containing no nuclei. The thickness of this layer varies enormously in direct proportion to the amount of friction or trauma to which the part of skin is subjected These cells are detached and shed.

The normal buccal mucous membrane possesses no granular or horny layers. The epidermal cells in their upward movement become vacuolated then shrink and are shed.

Lymph circulates between the cells of the lower reaches of the epidermis, but there are no lymph or blood vessels nerve fibres and Merkel s discs (touch receptors) are demonstrable.

THE EPIDERMAL APPENDAGES

The sweat glands (eccrine glands) are present in all parts of the skin, but most abundantly in the palms, soles and axillae They produce a liquid secretion containing no cellular substance The sweat gland is a long blind tubule consisting of a spherical, coiled secretory part situated deep in the dermis or at the dermo-hypodermal junction and a duct which cork screws upwards through the dermis and epidermis to open on the surface. The secretory portion of the gland is composed of an inner layer of cylindrical secretory cells and an outer layer of spindle-shaped myoepithelial cells which are contractile and drive the secretion into the lumen. The duct is composed of two layers of cuboidal cells and appears to maintain its identity even as it passes through the epidermis (Figs. 4 and 5)

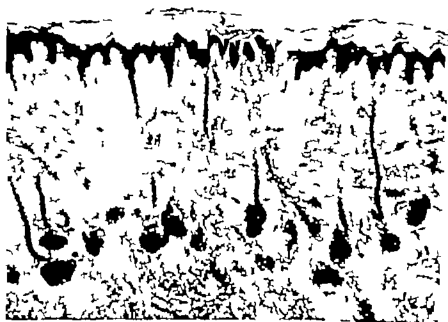


Fig. 4
Eccrine sweat glands and ducts.

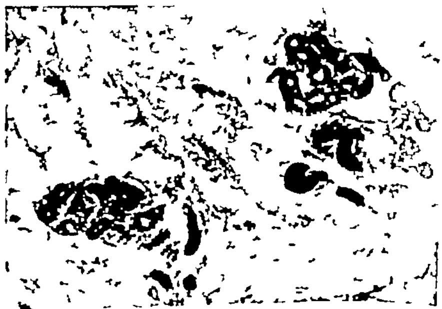


Fig. 5
Eccrine sweat glands.

The apocrine glands originate from the primary epithelial germ and their ducts lead into pilo-sebaceous follicles and not direct to epidermis like those of sweat glands. They are vestigial scent glands and are found only in the axillae, around the nipples and in the genital region modified apocrine glands are the ceruminous glands of the ear Moll's glands of the eyelids and the mammary glands.

Apocrine glands are tubular but the lumen of the secretory portion is ten times larger than that of a sweat gland. The

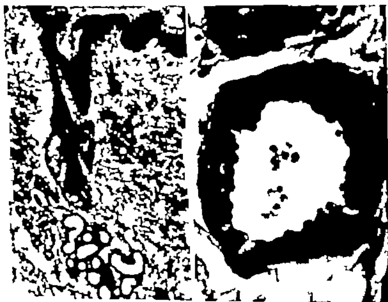


FIG. 6
Apocrine glands.
[H. W. Weber]

secretory portion is two layers thick, the outer layer being of myoepithelial cells. The inner layer is of cuboidal cells that protrude into the lumen and release part of their cytoplasm there (Fig 6)

The sebaceous glands are alveolar holocrine glands whose secretion, sebum, is formed by cellular decomposition. They are found all over the skin and genital mucosa except on the palms and soles, and modified forms are found in the lips

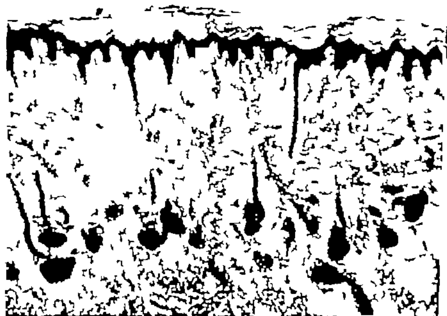


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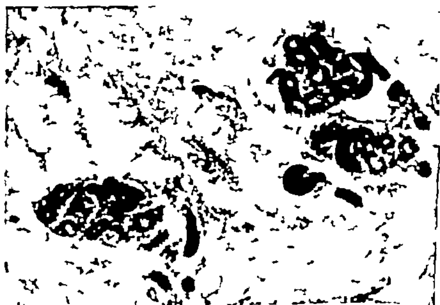


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as Fordyce's glands and in the eyelids as the Meibomian glands One to six glands are clustered round each pilo-sebaceous follicle into which they discharge. Each gland has several lobules with a peripheral layer of cuboidal generative cells that contain no lipids The cells within the lobule are arranged in a delicate network and are filled with fat These are the cells which finally break up into an amorphous fatty mass that diffuses upwards into the follicles and mixes with the eccrine sweat to form a surface film (Fig 7)



FIG. 7
Hair follicle sebaceous gland and arrector pili.

The hair consists of a bulb of hair matrix cells lying in the dermis or hypoderm, a root consisting of non keratinized cells and a projecting shaft of keratinized cells Into the bulb goes a papilla of connective tissue containing blood vessels and nerves, and melanin in dark haired people A hair has tv inner sheaths developing from the matrix cells and an out r sheath of downward-growing epidermis Each hair proje ts from a follicle which is an invagination of the skin sebaceou glands discharge into the depths of the open funnel-shap l part of the follicle.

The hair is constantly being renewed soft lanugo hair and eyelashes have a short life of about five months, but that of scalp hair is three to five years. The old papilla ruptures and a new one forms and the new hair grows alongside the old one in the follicle until it is shed.

The nails are composed of keratin and are formed by the nail matrix which lies under the attached end of the nail and extends forward under the lunule Neither the nail matrix nor the nail bed beyond it have any stratum granulosum. The growth of a nail from matrix to free end takes about six months.

THE DERMIS

The dermis is a fibro-elastic layer that contains blood and lymph vessels, epidermal appendages, muscle and nerve



FIG. 8
Collagen and elastic fibres in normal skin. Elastic fibres are black.
Henry Haber

elements. Its uppermost part consisting of the papillae that project into the epidermis is known as the papillary layer under this is the reticular layer Collagen, elastic and reticulum fibres, enveloped in a ground substance are the main elements of the dermis (Fig 8)

Collagen fibres make up 98 per cent of the connective tissue and form bundles bound by ground substance. The bundles are irregularly disposed in the upper dermis but lie parallel to the surface in the lower reaches Fibroblasts are sparsely scattered between the collagen bundles.

Elastic fibres run mainly parallel to the surface in wavy lines among the collagen bundles and are most numerous in the lower parts of the dermis They play no part in the dermo-epidermal attachment Elastic tissue is ill named as it is rigid this rigidity prevents overstretching and helps to restore skin to normal after it has been stretched

Reticulum fibres are revealed only by silver staining and are not present in large quantity in normal skin They form a fine network (*gitterfasern*) running from the epidermis (where they interdigitate with cytoplasmic processes of the basal cells) to the glands and blood vessels. Reticulum fibres are seen in large quantities in chronic infective granulomatous diseases such as tuberculosis and in many of the reticulo-endothelioses They probably arise from precipitation of an extracellular excretion of mesodermal cells such as reticulum cells, histiocytes lymphocytes and endothelial muscle and fat cells. Reticulum is a precursor of collagen

Nerves Sensory nerves and end-organs of the cerebrospinal system are found in the dermis and nerves of the autonomic system supply the blood vessels, smooth muscles and sweat glands Sebaceous glands have no nerve supply and are under hormonal control

Blood vessels There is a deep plexus of arterioles at the lower border of the dermis and a superficial capillary plexus in the subpapillary region that sends branches up into the papillae

A special structure concerned with temperature control by short-circuiting an arteriole to a venule bypassing the capillaries, is known as the glomus Glomus bodies are seen particularly in the toes, fingertips and nailbeds An arterial segment, the Sucquet Hoyer canal, branches off an arteriole and has a narrow lumen and a thick wall. The wall is lined by endothelial cells around which are large clear contractile glomus cells probably derived from pericytes Among the cells goes a network of nerve fibrils The venous segment has a wide lumen and leads to a subpapillary venule

Lymph vessels Lymph circulates between the basal and Malpighian cells of the epidermis and between the collagen bundles. Lymph vessels largely follow the distribution of the blood vessels.

Muscles Smooth muscle is found in the skin as the arrectores pilorum, the dartos muscle of the scrotum and in the nipple areola. The arrectores pilorum, best developed in the scalp, run from the papillae and below the sebaceous glands to the hair follicle In contraction they pull the hair vertical and produce gooseflesh Striped muscle is found in the neck and face.

Cellular elements Some cells of the reticulo-endothelial system are seen in normal skin Histiocytes are present in small numbers as perithelial cells around the capillaries. They may migrate in pathological states and phagocytize foreign particles or microbes and are then known as macrophages. They may take up melanin and are then known as melanophores. Fibroblasts and mast cells are also present in normal skin. The potentialities of the cells of the reticulo-endothelial system are considered in Chapter XXV

PHYSIOLOGY

The skin is the largest organ of the body and it performs a number of functions, some essential to life, which may be summarized thus. It is firm, elastic and resilient and acts as a barrier against physical, chemical and microbic trauma. It regulates the body temperature by means of the sweat glands and blood vessels. It secretes water as a means of temperature control, and sebum which insulates and lubricates the surface and contains antimicrobic principles and precursors of vitamin D It contains nerves which appreciate pain, heat, cold and touch.

CHEMICAL CONSTITUENTS OF THE SKIN

Water is an important constituent of the skin The elasticity of the stratum corneum depends on its water content more than on the surface sebum whose main effect is probably insulation and prevention of water dissipation rather than lubrication

Electrolytes are found mainly as chlorides of sodium potassium magnesium and calcium

Carbohydrates are found as glucose, glycogen and complex glucides Free glucose exists in lower concentration than in the blood When augmented in diabetes it facilitates the growth of micro-organisms on the skin

Glycogen is found in the stratum Malpighii and in the glands of the skin It takes part in the elaboration of keratin and is found in increased quantity in some inflammatory and neoplastic states The complex glucides mucopolysaccharides are of prime importance in the dermis

Lipids are found intracellularly as sterols in particular cholesterol and phospholipids Fatty acids are found in intercellular distribution.

Proteins of both globular and fibrous structure are found in the skin Sulphydryl amino acids are important constituents of skin proteins

PERMEABILITY

The skin is essentially impermeable to non-gaseous substances This impermeability is dependent on a number of factors The keratinous stratum corneum offers some protection against penetrants and its removal facilitates penetration The oily surface film impedes the entry of volatile substances Undamaged skin behaves like a membrane with a negative electric charge and this property which probably resides at about the level of the stratum granulosum, doubtless plays a part in the repulsion of water and dissociated electrolytes

Transcutaneous absorption of certain substances does take place through undamaged skin, either through the epidermis or *via* the pilo-sebaceous follicles Penetration by water is negligible and medication is accomplished by the use of fatty and fat-solvent vehicles Water-soluble substances are little absorbed but some lipo-soluble substances pass easily Penetration by ointments may be facilitated by previous cleansing with fat solvents or by the use of keratolytics

A surface film covers the skin It is an emulsion composed of water and water-soluble substances derived from eccrine sweat and fatty components from the sebaceous glands and to a minor extent, from the apocrine sweat glands it also contains

degeneration products of the stratum corneum and a precursor of vitamin D

The surface film offers some protection against chemical insult and has fungistatic and bactericidal properties. Fatty acids derived largely from the sebum are probably the active antimicrobic principles, but the acidity of the skin, the "acid mantle" is believed by some also to be involved. The *p*H of the skin varies between 4·2 and 5·6 in different areas. Dilute acids and, to a lesser degree, dilute alkalis are neutralized to a certain extent on the surface.

TEMPERATURE REGULATION

The skin acts both as an insulator and as a dissipater of heat. A certain amount of heat loss takes place by radiation and by conduction to the air but the most important way in which heat is lost is by the secretion and evaporation of sweat. The state of dilatation or constriction of the blood vessels is also important. In vasoconstriction the glomus organs come into function as arterio-venous shunts so that the capillaries are bypassed and heat loss diminished.

THE EPIDERMIS

The epidermis contains two distinct cell types, the melanocytes which are concerned with melanin pigment formation and are found between the cells of the stratum basale, and the epidermal cells proper whose main function is the manufacture of keratin. The epidermal cells are part active, part dead and the epidermis is in constant outward growth as cellular division takes place in its lower reaches and the dead cells of the stratum corneum are shed. The upward progression of the cell from the stratum basale is accompanied by change of shape, content and vitality and its final form is a cell wall filled largely with keratin. Cellular density and compactness increases from below upwards as the state of intra- and extracellular hydration decreases. Mitotic division is evident in the cells of the stratum basale and in the deeper layers of the *stratum Malpighii*. The cells are dying in the stratum granulosum and it is probable that the granules of keratohyalin are products of nuclear degeneration since they are chemically unrelated to keratin.

The process of keratinization begins deep in the stratum Malpighii and is normally complete in the stratum corneum The globular cellular proteins are transformed to fibrous proteins and a prime reaction in this transformation is the oxidation of the sulphydryl amino acid cysteine to cystine The energy for the reaction is furnished by glycogen which disappears from epidermal cells as keratinization proceeds

Keratin is a fibrous protein with a very long and very narrow molecule Molecules are arranged in parallel and joined by cross linkages which bond them but allow a wide range of elasticity These linkages are of various types disulphide bridges are strong and resistant to physical and chemical stresses, salt and hydrogen bridges are more labile Keratin is insoluble in water strong acids, dilute alkalis and solvents and resistant to digestion by trypsin and pepsin Some fungi have a keratinase which digests keratin molecules

The hard keratin of nails and hair differs from the soft keratin of the stratum corneum in having a higher sulphur content which may account for the closer bonding Keratin normally exists in the alpha form with its molecules folded and crinkled stretching straightens the molecules into the beta form which will revert to the alpha when tension is released The altered shape of stretched keratin can be maintained if the cross linkages are broken Reducing agents and strong alkalis attack the disulphide bridges This effect is used in cold permanent waving where a reducing agent ammonium thioglycolate is used and permits the manipulation of the hair to a desired shape oxidizing agents are then applied to restabilize the keratin molecules Strong alkalis as keratolytics have a practical use in the examination of epidermal scales, nail or hair for fungi Barium sulphide is used as a keratolytic in depilatory preparations Salicylic acid and resorcinol have a minor keratolytic effect by acting on the hydrogen bridges

Keratin can hold water and the state of hydration of the stratum corneum is of more importance in its elasticity and resiliency than is its fat content. The oestrogens increa keratinization while vitamin A has an inhibitory effect

THE GLANDS OF THE SKIN

The sebaceous glands Sebaceous glands are found all over the body except in the palms and soles, but are most numerous on the scalp and face and near the midline of the back and chest. The secretion of the glands, sebum, is an oily fluid produced by the total disintegration of the gland cells and is composed of free and combined fatty acids, cholesterol, squalene, a precursor of vitamin D and other components. Sebum diffuses through the pilo-sebaceous follicles on to the skin surface where it forms an emulsion with the sweat.

The secretion of sebum is not directly under nervous control, but the hypothalamic centres probably act indirectly on the sebaceous glands by way of the ductless glands. Sebum secretion is augmented when the surface film is removed by solvents or made more fluid by sweating

The sebaceous glands of the child are inactive, but puberty brings them into action and even, for a time until normal adult gonadal hormone secretion is established, into overactivity Testosterone and progesterone stimulate the sebaceous glands, oestrogens have an inhibitory effect. The acneoid reaction seen sometimes in patients treated with ACTH or cortisone is due to follicular hyperkeratosis and not to sebaceous glandular hyperplasia.

The fatty acids of sebum have some bactericidal and fungistatic action which explains the frequency of epidermophyton infections on the feet, which are devoid of sebaceous glands, and the spontaneous healing of *Microsporon audouini* infections of the scalp at puberty when the glands come into full function. The importance of provitamin D in human sebum has not been assessed.

The apocrine glands These glands, vestigial in the human species, are related more closely to the sebaceous than to the sweat glands and deliver their secretions into the pilo-sebaceous follicles. They are most numerous in the axillary ano-genital and nipple areas. They come into activity at puberty and are better developed in women than in men. Secretion in women is augmented in the premenstrual period and diminished in pregnancy and after the menopause.

Apocrine sweat is composed partly of products of cellular degeneration, partly of a fluid, eccrine secretion which is

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then formed is of the soft variety and heaps up under the nail plate and elevates it. Deformities in the plate itself are usually caused by disease in the matrix. The rate of nail growth is stimulated by elevation of temperature (summer more than winter) and by persistent erosion or removal of the free end

The life of a hair is divided into two phases, a growing phase (anagen) and a resting phase (telogen) A scalp hair has a total life of several to many years hair in other areas only a few months. The growing phase is long, the resting phase brief. In the resting phase the hair matrix no longer produces keratinized cells, but only undifferentiated epithelial cells which push upwards in a column that carries the resting or club hair nearer the surface. Finally a new bulb forms a little above the site of the original bulb and a new hair grows upwards into the follicle alongside the resting hair if this has not already been shed

The rate of growth of hair varies from 0 1 to 0 4 mm per day and is most rapid in the beard and scalp growth is faster in summer than in winter and in the day than in the night.

The sex distribution of hair is governed by the androgens the oestrogens have little effect on hair growth. Paradoxically male castrates do not develop the ordinary male type of baldness unless they are given androgens. Hyperplasia of the adrenal cortex, with increased androgen production, whether spontaneous or induced by ACTH, has a virilizing effect in women, as has the administration of androgens. Hypopituitarism leads to diminution of secondary sex hair Hair loss is a characteristic feature in myxoedema, but the mechanism is not clear

The growth of hair is little affected in chronic malnutrition and vitamins have no effect on any type of alopecia.

THE DERMIS

The dermis is the largest and most important layer of the skin In most areas it is very much thicker than the epidermis, with an average of about 3 mm. as against 0·2 mm. Its function is protective against external injury and supportive for the blood vessels, nerves and epidermal appendages. It has a large capacity for fluid storage both within and without the blood vessels. Fibrous and cellular components lie in an

stimulated by the sympathetic nervous system Apocrine sweating is seen in response to emotional stimuli and is not provoked by heat

The sweat is milky and contains carbohydrate fatty and nitrogenous constituents, iron and chromogens which may on oxidation impart colour (of bluish tints usually) to the fluid. The odour of axillary sweat is a result of bacterial decomposition of apocrine sweat which when secreted is sterile and odourless

The eccrine sweat glands Eccrine sweat glands are found all over the body and by the secretion of a watery sweat they play the chief role in temperature regulation The centre for sweat control is in the hypothalamus and increase of blood or skin temperature triggers the secretion Sweating also occurs as a result of emotional stimuli when it is most marked on the palms, soles axillae and forehead or in certain people after eating certain foods (gustatory sweating) when the centre of the face is affected With the body at rest there is still secretion of sweat, but it is not apparent to the eye and only a certain percentage of the glands are working at any given time

Sweat secretion is initiated by stimuli reaching the glands *via* the sympathetic nervous system and mediated by acetyl choline there is no nervous inhibition of sweat gland activity Sweating is induced by pilocarpine and suppressed by atropine and banthine

Eccrine sweat is an acid fluid consisting largely of water but containing mineral salts (potassium chloride particularly) urea uric acid and other nitrogenous compounds, glucose and lactic acid The role of the sweat glands as excretory organs is, however negligible

Nails and hair Both of these epidermal structures are, in man largely vestigial They enhance the sensation of touch but their original protective and insulating (hair) qualities are unimportant Both are to a very large extent, uninfluenced by any form of medication and the mechanisms involved in most of the diseases that affect them are poorly understood if they are understood at all

The nail plate grows forward from a formative epidermal matrix over a nail bed to which it is firmly attached The nail bed manufactures keratin only in disease states and the keratin

then formed is of the soft variety and heaps up under the nail plate and elevates it. Deformities in the plate itself are usually caused by disease in the matrix. The rate of nail growth is stimulated by elevation of temperature (summer more than winter) and by persistent erosion or removal of the free end

The life of a hair is divided into two phases, a growing phase (anagen) and a resting phase (telogen) A scalp hair has a total life of several to many years hair in other areas only a few months. The growing phase is long the resting phase brief. In the resting phase the hair matrix no longer produces keratinized cells, but only undifferentiated epithelial cells which push upwards in a column that carries the resting or club hair nearer the surface. Finally a new bulb forms a little above the site of the original bulb and a new hair grows upwards into the follicle alongside the resting hair if this has not already been shed.

The rate of growth of hair varies from 0 1 to 0 4 mm. per day and is most rapid in the beard and scalp growth is faster in summer than in winter and in the day than in the night.

The sex distribution of hair is governed by the androgens the oestrogens have little effect on hair growth. Paradoxically male castrates do not develop the ordinary male type of baldness unless they are given androgens. Hyperplasia of the adrenal cortex, with increased androgen production, whether spontaneous or induced by ACTH, has a virilizing effect in women, as has the administration of androgens. Hypopituitarism leads to diminution of secondary sex hair Hair loss is a characteristic feature in myxoedema, but the mechanism is not clear

The growth of hair is little affected in chronic malnutrition and vitamins have no effect on any type of alopecia.

THE DERMIS

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which show regularly spaced transverse striations, some dark and some light, like the markings on striped muscle

Collagen fibres are composed of amino acids in polypeptide chains cemented by chondroitin-sulphuric acid the molecular form permits of the absorption of much water

Elastic fibres are found throughout the dermis in much smaller numbers than collagen fibres Their fine structure is quite different from that of collagen Electron microscopy shows an elastic fibre to consist of two pairs of fibrils rolled in a spiral and showing no striations. The origin of elastin is disputed some postulate its formation by elastocytes, others believe that it is altered collagen.

The ground substance of connective tissue is a demi-gel or demi-sol and is in the most intimate and inextricable relationship to the fibrous elements. It is composed of substances derived from the circulation (water glucose, proteins, inorganic ions) metabolic products of parenchymatous cells and metabolic products of the connective tissue itself (mucopolysaccharides such as chondroitin-sulphuric acid, hyaluronic acid and protein-mucopolysaccharide complexes) The ground substance is the intermediary for exchanges between the blood stream and the parenchymatous cells and the lymph derives from it.

Alterations in the ground substance are involved in the so-called collagen diseases, amyloid disease, myxoedema, etc.

The blood vessels of the dermis are concerned in body temperature regulation, in metabolic processes, in defence against trauma and infection and in processes of repair The amount and colour of the blood in the venules is largely responsible for the tint of the white skin. The sympathetic nervous system innervates the arterioles and glomus organs and stimulatory impulses keep the arterioles in a state of constriction there are no vasodilatory fibres. Adrenaline and noradrenaline cause vasoconstriction acetylcholine and histamine cause vasodilation and they are probably involved as chemical intermediaries in vascular reactions caused by nervous impulses.

Local reflex vascular reactions independent of the central nervous system also occur in response to heat, cold or trauma. These reactions depend on direct stimulation of arteriolar muscle or on the traumatic release of acetylcholine or histamine

amorphous ground substance It is suggested that the living dermis is in fact a gel and that the fibrous appearance is produced by the substances used in preparation of specimens for histological examination

Cellular elements are few in the normal dermis The three cell types are all derived from the primitive reticulum cell and are so similar that they are difficult to distinguish in routinely stained sections It is probable that they may be transformable one to the other

Fibroblasts are the most important and are sparsely scattered among collagen fibres From them originate the reticulum fibres which are the precursors of collagen This function is inhibited by cortisone and by vitamin C deficiency

Histiocytes are similar to and closely related to fibroblasts but differ in being mobile and possessing the capacity for phagocytosis They are hard to recognize in normal skin and are found mainly around the capillaries

Mast cells are recognizable only by special staining techniques, such as toluidine blue which show their cytoplasm to be full of metachromatic granules In the granules are elaborated or stored histamine heparin 5-hydroxytryptamine and a precursor of hyaluronic acid These substances affect the state of dilatation and permeability of the capillary walls and are released in inflammatory states or after trauma

It seems probable that the most important element in the dermis, and in all connective tissue, is the ground substance and that the fibrous elements are formed from it by the fibroblasts. The three varieties of fibres are distinguished by their tinctorial properties and by their reactions to enzym[illegible] action

Reticulum or reticulin fibres are present in very small quantity in the normal dermis and are generally accepted as being the precursor of collagen. Electron microscopy shows them to have the same appearance as those of collagen though they are finer and they give the same spectrographic picture as collagen

Collagen forms the major part of the dermis The name derives from the fact that a gluey substance gelatin [illegible] formed when collagen is boiled in water Under the electron microscope collagen fibres are seen to be composed [illegible] anastomosing fibrils, themselves composed of m[illegible] fibril

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SENSATION IN THE SKIN

The sensations of touch pain heat and cold are appreciated by a vast number of fine sensory nerve endings in the dermis and epidermis Doubt has been thrown on the authenticity of the various nervous end organs which were reputed to perform specialized functions in regard to these sensations some at least are now believed to be artefacts

Itch or pruritus is often described as pain in miniature and many painful stimuli will in lower intensity cause itch medicinal and physical palliatives for pain do not however always allay itch Some light has recently been thrown on the causative mechanism of itch by experiments with itch powder which consists of the barbed hairs (trichomes) from the pods of cowhage (*Mucuna pruriens*) These trichomes contain a proteolytic enzyme, mucunain which is apparently the active principle in causing the itch when it is introduced into the skin if the enzyme is inactivated by autoclaving the trichomes, no itch ensues when they penetrate The scope of the experiments made it unlikely that histamine release played any part in causing the itch Other enzymes were studied and it was shown that itch was caused by endoproteinases active within the physiological range of pH (e g papain trypsin pancreatin) It is possible, therefore, that itch is caused by release of proteases from the cells of the skin as a result of a variety of noxious stimuli

The varying capacity of different people to itch is an obvious but inexplicable phenomenon psychological factors have only minor importance The variations in sensitivity are extreme and are easy to study in scabies most patients itch some intolerably but a few may be covered with lesions and have little or no discomfort

The motor nerves in the skin are derived from the sympathetic and supply the musculature of the arterioles, the arrectores pilorum the myoepithelium of the apocrine and eccrine sweat glands and the glands themselves

THE HYPODERM

The basic cell of the hypoderm is the lipocyte which manufactures and stores fat Lobules of lipocytes are separated by strands of collagen and elastic fibres The quantity and

quality of the hypodermic fat varies from one part of the body to another and is distributed differently in the sexes.

The hypoderm acts as a heat insulator as a cushion against trauma, and as a food reserve. Starvation depletes the hypoderm, but the fat is spared in places where it serves an important protective purpose as in the palms and soles The hypoderm in thick skin grafts continues in its new situation to behave as it did in its original site e.g transplanted abdominal skin will fatten in tune with the ordinary abdominal skin.

The hypoderm contains vessels, nerves, epidermal adnexae and muscle striped muscle is found in the face and neck, unstriped muscle in the scrotum and nipples.

Skin pigment

The colour of the human skin depends mainly on the quantity of pigment within it. The pigment of greatest importance is melanin which is formed in the melanocytes (clear cells) of the basal layer of the epidermis. In the normal white skin melanin is found mainly in this region in the melanocytes and their dendritic processes. In dark-skinned races melanin can be seen in the upper layers of the epidermis and in mesodermal phagocytic melanophores (histiocytes) It has been demonstrated that the epidermal melanin is contained within dendrites of melanocytes and not in basal or Malpighian cells in the strata granulosum and corneum free melanin granules occur

The presence of melanin itself is demonstrated by silver stains, but only the melanocytes are stained by the dopa reaction (Bloch) which shows their capacity to manufacture melanin whether they happen to contain it at that moment or not. Melanocytes stain dark because they contain an enzyme, tyrosinase, which changes colourless dopa (l 3, 4, –dihydroxy phenylalanine) into dark, insoluble dopa melanin. Melanophores are not stained by the dopa technique Apart from the basal layer of the epidermis melanocytes are found only in the hair bulb, but the mechanism of hair pigmentation is apparently not the same as that of the skin.

In the melanocytes of the skin is a copper-containing enzyme tyrosinase, which can convert tyrosine to dopa in the presence of molecular oxygen. Once the reaction has started

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effects. Immediate pigmentation, or pigment darkening a phenomenon seen on most dark skins and many white ones a few minutes after exposure to sunshine, is probably due not to melanogenesis, but simply to oxidation of reduced (leuko-) melanin.

The hormonal control of melanogenesis appears to be exercised principally by the pituitary gland under the influence of other glandular disturbances. The pituitary gland secretes a melanocyte stimulating hormone (MSH) which has been isolated and which may occur as a contaminant in ACTH. The use of contaminated ACTH produces hyperpigmentation which is especially marked in those areas affected by skin lesions of an allergic nature (e.g. erythema multiforme): the phenomenon is most marked and seems to me to occur oftenest on black skins. Injection of pituitary extracts containing much MSH into test subjects produces darkening of skin and of naevi and sometimes the appearance of fresh naevi.

Hydrocortisone probably inhibits the release of MSH, and adrenalin and noradrenalin from the adrenal medulla and adrenergic nerve endings and may reduce or prevent the action of MSH on melanocytes. In adreno-cortical insufficiency (Addison's disease) decreased output of hydrocortisone provokes a compensatory increase in pituitary activity and secretion of MSH and ACTH. If the adrenal medulla were also affected MSH would no longer be peripherally inhibited by adrenalin. Cortisone and hydrocortisone can prevent hyperpigmentation in patients with Addison's disease or bilateral adrenalectomy.

Oestrogens are probably involved in the normal and abnormal increase of pigmentation in certain areas during pregnancy. Hyperpigmentation may occur in states of hypo- or of hyperthyroidism. Eunuchs tan poorly except when they are given testosterones.

The depigmentation of vitiligo and albinism seems to be due to some defect in the system of melanogenesis because melanocytes are present though inactive. Removal of the epithelium by blistering or by the dermatome in vitiliginous patches may be followed by a temporary repigmentation, presumably from melanocytes migrating from the hair follicles in the process of healing. This is another illustration of the

dopa itself acts as an accelerator Dopa is transformed to dopaquinone and that in turn to indolic compounds before melanin is finally synthesized It is suggested that melanin may be 5, 6 -hydroxyindole α-carboxylic acid Tyrosinase exists in a state of inhibition in normal skin but is activated by actinic rays and endocrine influences The process of melanin production can be influenced and controlled by various factors.

The tyrosine tyrosinase reaction is accelerated by many substances including dihydroxyphenyl compounds of these dopa is the most effective. Tyrosinase is inhibited by sulphydryl compounds such as glutathione and cysteine which combine with its copper component. Such natural compounds may well play a part in controlling melanin formation. It is suggested that arsenical pigmentation may be due to binding of sulphydryl compounds in the skin by arsenic thus freeing tyrosinase from their inhibitory action Reducing agents such as ascorbic acid inhibit oxidation of tyrosine by tyrosinase Ascorbic acid reduces pigmentation in Addison s disease this effect may be due to inhibition or to reduction of melanin to the lighter coloured melanoid Exposure of ascorbic acid to ultraviolet light or x rays oxidizes it so it is possible that the vitamin may be involved in natural melanogenesis Ascorbic acid plays a major role in the maintenance of SH levels in blood and tissue Hyperpigmentation may occur in scurvy

Melanin formation may be inhibited by the ingestion of certain sulphur-containing compounds such as thiouracil and dimercaprol (BAL) which bind copper Local application of parahydroxyphenyl derivatives may depigment negro or hyperpigmented white skin an important member of this group is monobenzyl ether of hydroquinone (agerite alba) and it is interesting to note that in areas depigmented by this substance the hairs are not affected. Agerite alba is used therapeutically to reduce pigmentation but it must be used continually or the pigment will return Its mode of action is uncertain and it will not always work a personal possibly allergic, factor may be involved

It seems probable that the pigmentation following exposure to actinic rays, x rays, etc. is due to oxidation or destruction of sulphydryl compounds and possibly ascorbic acid in the skin and the consequent release of tyrosinase from their inhibit[illegible]

CHAPTER II

BASIC CHANGES

HISTOPATHOLOGICAL CHANGES

The basic pathological changes in the skin may be summarized as functional, inflammatory degenerative and proliferative or neoplastic. Many of the patterns of pathological change are graced by names which are here explained In most diseases it is usual to find a variety of changes which may be confined to only one major layer or involve the whole depth of the integument.

The epidermis

Hyperkeratosis implies an abnormal thickening of the stratum corneum. It may be caused by reduced shedding of the superficial cells as in ichthyosis vulgaris or by increased production of keratin as in calluses. The stratum granulosum is also thickened when increased keratin formation is involved Hyperkeratosis may be a relatively or widely generalized process or it may be strictly localized to follicular or glandular orifices (Fig 9)

Parakeratosis consists in the formation of imperfectly keratinized cells in the stratum corneum. These cells retain their nuclei. The stratum granulosum is absent in such areas. This change is well illustrated in psoriasis, but occurs in many dermatoses

Dyskeratosis is an imperfect and premature keratinization of individual cells in the epidermis. Benign dyskeratosis is seen in Darier's disease and familial benign chronic pemphigus, malignant dyskeratosis in intra-epidermal carcinomas such as Bowen's disease and in squamous-cell carcinoma (Fig 10)

Hypergranulosis defines an increase in the number of cells in, and thickness of the stratum granulosum such as is seen in lichen planus.

difference between melanogenesis in hair and skin the migrating hair melanocytes eventually behave as skin melanocytes and any pigment disappears again The possibility of neurogenic influences in melanogenesis is suggested by the observation that normal skin transplanted to a vitiliginous area becomes depigmented while vitiliginous skin regains its pigment when transplanted to a normal area

The use of certain histochemical and biochemical techniques such as those of Fitzpatrick and Lerner allow the estimation of tyrosinase activity in histological preparations and in gross tissue. Activity is greatly increased in malignant melanoma whether pigmented or achromic and refinements of these tests may prove valuable for differential diagnostic purposes

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Fig 9

Top Hyperkeratosis, hypergranulosis and acanthosis lichen planus.
Bottom Parakeratosis and spongiosis in pityriasis rosea.

[M. Reeves (?)]

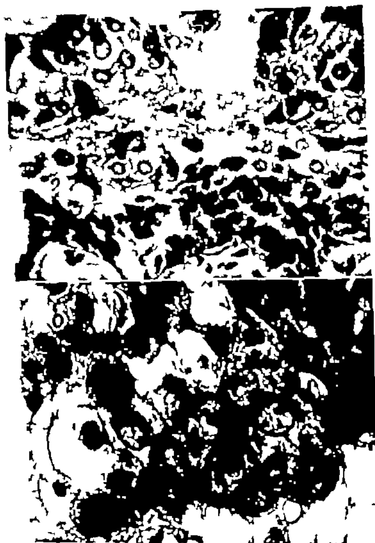


FIG. o.

Top Dyskeratosis in familial benign chronic pemphigus.
Bottom Acantholysis in pemphigus vulgaris.

[M. Ramler]

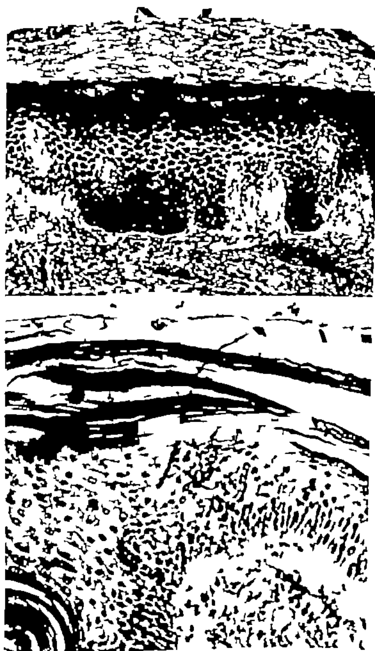


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(M. Rieter (?)





Fig.

Top. Acanthosis and papillomatosis in chronic eczema.
Bottom. Atrophy of epidermis in acrodermatitis chronica atrophicans.

[illegible]

Acanthosis (hyperacanthosis) is an increase in thickness of the stratum Malpighii It occurs in a great variety of diseases (Fig 11)

Acantholysis means the dissolution of the intercellular bridges between the cells of the stratum Malpighii as well as those of the stratum basale It leads to the formation of vesicles and bullae. It occurs in pemphigus vulgaris, familial benign chronic pemphigus, Darier s disease virus bullae senile keratoses and congenital ichthyosiform erythroderma.

Balloon cells are swollen degenerate Malpighian cells seen in virus infections The intercellular bridges are disrupted and this leads to the formation of multilocular vesicles or bullae (reticular degeneration)

Spongiosis is an intercellular oedema that separates the cells of the stratum Malpighii without totally disrupting the intercellular bridges It occurs in inflammations of the skin especially eczema and dermatitis

Altération cavitaire is intracellular oedema of Malpighian cells which may lead to their disruption and the formation of multilocular spaces (reticular degeneration)

Liquefaction degeneration of basal cells In a number of diseases including lupus erythematosus, lichen sclerosus et atrophicus and incontinentia pigmenti the basal cells become vacuolized and disintegrate As a result, melanin may be released and drop into the upper dermis where it lies free and within macrophages. This phenomenon *incontinence of pigment* is characteristic of a syndrome of unknown origin incontinentia pigmenti but may occur in lupus erythematosus, lichen planus, etc.

Nuclear changes Death of a cell in the epidermis or elsewhere may lead to condensation of the nucleus *pyknosis* or to its fragmentation into small granules or dust *karyorrhexis*

In *atrophy of the skin* as a result of pressure from without or within from age or from sensory nervous changes, the epidermis is thinned keratin formation diminished and the dermo-epidermal line of junction is straightened out

THE DERMIS

A variety of pathological alterations of the fibrous elements and of the ground substance of the dermis may occur some are

Infiltration of the dermis by cells not normally encountered there is a common phenomenon and the character of the infiltrate may be of diagnostic significance Polymorphonuclear leucocytes are found in acute inflammatory and infective states, while lymphocytes predominate in healing lesions and in chronic, granulomatous conditions. Eosinophils are prominent in the infiltrates caused by some allergic and other diseases. The distribution of the infiltrate, band like

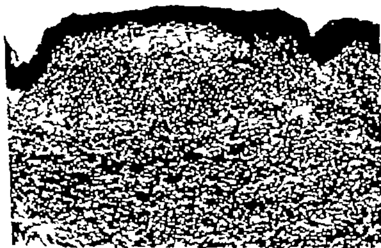


FIG. 3

Band-like infiltrate in dermis in lichen planus.

[W. Freudenthal]

in the papillary layer of the dermis, is noteworthy in lichen planus (Fig 13)

The infective granulomas (tuberculosis, leprosy syphilis, deep mycoses) are characterized by an infiltrate of cells of the lympho-reticular series, some of which (histiocytes, mast cells, fibroblasts) are normally found in the dermis and others (epithelioid cells, giant cells, lymphocytes, plasma cells) which are intruders. The architecture of the infiltrate may be a pointer to the diagnosis.

The histiocyte functions as a phagocyte and may ingest melanin (the melanophore of the normal and abnormal

evident in routinely stained specimens and some are demon strated only by special staining techniques



FIG. 2

Top Elastorrhexis in acrodermatitis chronica atrophicans.
Bottom Reticulum fibres in solitary mastocytoma.

The collagen and elastic fibres may show either hyper trophic or degenerative changes. Reticulum fibres, sparse in the normal dermis, are increased in some inflammatory states and in diseases of the reticulo-endothelial system (Fig 12)

dermis) lipids (foam cell) small particles of foreign matter of endogenous or exogenous origin and micro-organisms of all varieties. When histiocytes cannot individually cope with a foreign body they may cluster about it and fuse to make foreign body giant cells. Epithelioid cells are altered histiocytes and by amitotic nuclear division they may become giant cells of the Langhans type Multinucleate histiocytes filled with lipids, and known as Touton giant cells, are found in xanthomas.

Infiltrates composed entirely or predominantly of mast cells are found only in the mastocytoses (Fig 14)

Infiltrates composed of mature, immature and abnormal cells of the myeloid and lympho-reticular series are found in some cases of diseases of these systems.

The blood vessels may show hyperplastic, degenerative or inflammatory lesions that are often of value in diagnosis.

THE HYPODERM

Inflammatory changes (panniculitis) are very common, primary degenerative changes rare and neoplastic changes (lipoma, liposarcoma) banal or exceptional. Lesions of the blood vessels are common and easily distinguished, hence the importance of including a portion of the hypoderm when taking biopsy material (Fig 15)

STAINING METHODS AND DIAGNOSTIC MICROSCOPY

The standard staining method for skin sections is haematoxylin and eosin. This colours nuclei blue and cytoplasm, collagen, muscles and nerves pink.

Selective staining is used for the demonstration of certain normal or abnormal constituents of the skin. Only a few major examples will be cited and technical details must be sought in specialized works.

Collagen may be distinguished from muscle by the use of the following stains Mallory's aniline blue, Masson's trichrome and van Gieson's stains.

Elastic tissue stains black with Verhoeff's stain.

Reticulin fibres and neurofibrils stain black with Foot's stain.

Melanin stains black with silver stains. The presence of tyrosinase in melanocytes is demonstrated by Bloch's dopa reaction.

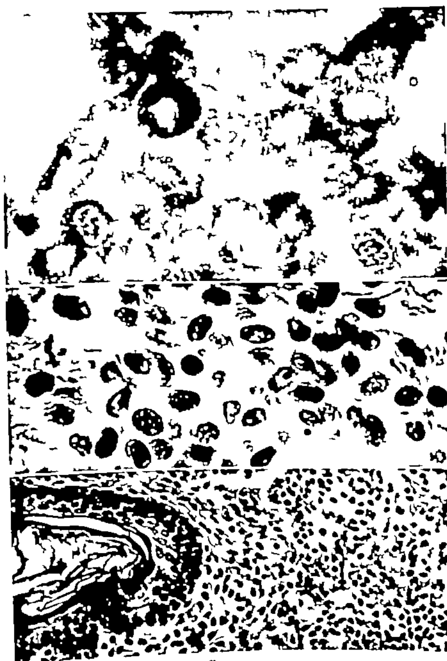


FIG. 4

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THE HYPODERM

Inflammatory changes (panniculitis) are very common, primary degenerative changes rare and neoplastic changes (lipoma, liposarcoma) banal or exceptional. Lesions of the blood vessels are common and easily distinguished, hence the importance of including a portion of the hypoderm when taking biopsy material (Fig 15)

STAINING METHODS AND DIAGNOSTIC MICROSCOPY

The standard staining method for skin sections is haematoxylin and eosin. This colours nuclei blue and cytoplasm, collagen muscles and nerves pink.

Selective staining is used for the demonstration of certain normal or abnormal constituents of the skin. Only a few major examples will be cited and technical details must be sought in specialized works.

Collagen may be distinguished from muscle by the use of the following stains Mallory's aniline blue, Masson's trichrome and van Gieson's stains.

Elastic tissue stains black with Verhoeff's stain.

Reticulum fibres and neurofibrils stain black with Foot's stain.

Melanin stains black with silver stains. The presence of tyrosinase in melanocytes is demonstrated by Bloch's dopa reaction.

Iron pigment stains blue with potassium ferrocyanide.

Micro-organisms The Giemsa Gram and Ziehl Neelsen techniques are employed for the demonstration and identification of bacteria Levaditi's stain for spirochaetes

Nerves are demonstrated by a variety of silver impregnations and by methylene blue

Mast cell granules become identifiable with toluidine blue and Unna's polychrome methylene blue



Fig 5

Vasculitis in the hypoderm in cutaneous periarteritis nodosa

(M Ender)

Lipids are stained red by Sudan III or Sudan IV (Scarlet red)

Amyloid is stained purple by crystal violet.

Mucin is stained red by mucicarmine.

Calcium stains black with von Kossa's stain

Glycogen and mucopolysaccharides are demonstrated by the Hotchkiss-McManus or periodic acid-Schiff stain This method is also useful in the investigation of fungous infections as the cell

walls of fungi stain sharply since they contain polysaccharides in much greater quantity than the normal skin components.

Desoxyribonucleic acid, present in nuclei and in many virus inclusion bodies, is identified by the Feulgen reaction.

Cytodiagnosis The examination of tissue smears or scrapings, especially from the floors of bullous lesions, is sometimes employed as a diagnostic measure, but is not to be considered as a substitute for biopsy which offers much more and much more accurate, information The May-Grunwald-Giemsa staining method is commonly employed.

Polariscopic examination, phase contrast microscopy historadiography autoradiography and electron microscopy are among other techniques used mainly with the exception of the first, in the experimental field.

THE ELEMENTARY SKIN LESIONS

A macule is a circumscribed discoloration of the skin without elevation, depression or palpable infiltration. The name is usually reserved for small lesions up to 1 to 2 cm. in diameter Macules may be caused by vasodilation, haemorrhage, pigmentary changes or foreign bodies in the skin.

A papule is a small solid elevation of the skin ranging in size up to 1 cm. in diameter Papules may be described as flat, conical, dome-shaped, squamous, follicular etc. They may be discrete or aggregated in groups. They may be caused by changes in the epidermis, the dermis or both

A plaque is a patch of altered skin The alteration may be one of colour alone or the skin may be elevated as a result of infiltration or oedema, or depressed from atrophy or fibrosis. The term is used only for lesions larger than 2 cm. in diameter

A nodule or tubercle is a solid elevation of the skin, with a base diameter of 1 to 3 cm due usually to dermal or hypodermal changes.

A tumour is a solid elevation of the skin larger than a nodule. Tumours may be pedunculated The term does not imply malignancy

A wheal (*urtica*) is a transient elevation of the skin due to dermal oedema.

Iron pigment stains blue with potassium ferrocyanide.

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Fig 15

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[W. Kinder]

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An ulcer is a loss of skin substance due to some cause other than trauma. The term usually implies a total loss of epidermis and of dermis or even hypoderm resulting from necrotic changes.

A scar is new-formed connective tissue replacing dermis or hypoderm destroyed by disease or injury

A vesicle is a collection of serous fluid either within the epidermis or between the dermis and the epidermis not exceeding 1 cm in diameter

A bulla is a collection of fluid larger in dimensions than a vesicle

A pustule is a superficial collection of pus within the epidermis or at the dermo-epidermal junction Pustules may arise *de novo* or from existing vesicles, bullae or papules.

An abscess is a collection of pus in the dermis or hypoderm that causes a fluctuant elevation of the skin.

Gangrene or *necrosis* is the death of a circumscribed part of the skin

The lesions just described are often called primary lesions as they may arise from previously normal skin Transition forms may be described as maculo-papular papulo-vesicular vesiculo-pustular lesions, etc. Changes supervening on these primary lesions produce the following secondary lesions

Scales are masses of epidermis resulting from over production of cells of the stratum corneum (hyperkeratosis) or interference with normal keratinization (parakeratosis)

A scab or *crust* is a dried mass of serum, pus or blood mixed with epithelial debris and perhaps bacteria When scabs form on actively developing lesions they may be deposited in layers that pile up one on the other to make hard thick shell like structures known as *rupia*.

An erosion is a superficial lesion produced by scratching or by the shedding of the upper layers of the epidermis as in the roof of an intraepidermal vesicle and causing loss of tissue extending into the stratum Malpighii. Such a lesion exudes serum

An excoriation is a traumatic lesion resulting from removal of the whole epidermal layer so that the dermal papillae are exposed these are seen in the floor of an excoriation as tiny bleeding points.

A fissure is a linear cleft or crack in the epidermis or epidermis and dermis. Fissures usually occur in normal skin folds and at points where movement is greatest when the skin is abnormally thickened and inelastic as a result of inflammation

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CHAPTER III

GENERAL PRINCIPLES OF DIAGNOSIS

A PATIENT with a skin disease should be examined first and interrogated later the patient's concept of the appearance of his lesions is irrelevant, and preliminary examination often drastically curtails the time spent on taking a history The patient should be examined in daylight and there is everything to gain by insisting on seeing all the skin a spot diagnosis of impetigo of the face in an adult may be changed to pustular secondary syphilis only if the patient is properly examined

The history is often of great importance but the patient's statements are not always to be taken at face value, for people with skin diseases rank high as misleading ill informed and wishful thinking witnesses, especially when a claim on the Workmen's Compensation Commissioner or some such third party is involved In taking the history the following lines, apart *from the obvious questions about age marital status etc* may have to be investigated

1 What is the patient's race? Where does he live now and where did he live in the past? Diseases of subtropical and tropical zones may develop after sometimes long after a patient has returned to temperate regions

2 What is his occupation and has he always been so employed? Ask for details of the type of work and materials handled when occupational dermatitis is suspected Patients should also be questioned about their hobbies

3 Is any other person in the patient's family household or place of occupation affected with a similar skin disease? This may give suggestive information in the case of inherited parasitic or occupational diseases

4 How and in what skin area did the disease begin? How did the disease evolve in relation to the lapse of time and to the nature of the lesions?

5. Has the patient previously suffered from similar or different skin diseases? Investigate also the past health history generally

6. Is there a history of allergic diseases (asthma, eczema, hayfever migraine) in the patient's family? This may be relevant in cases of atopic dermatitis.

7 What remedies, local or general, were used before the disease began or later for its treatment?

8 Did the onset of disease follow any change in habits (diet, cosmetics, new brands of soap etc.) clothing or general health?

9. The patient's views on the cause of his disease may occasionally be helpful.

The patient's *symptoms* in relation to the skin itself are seldom of diagnostic value

Itch of varying degrees of severity may accompany the majority of skin diseases. It is often constant and intolerable in erythroderma and other manifestations of diseases of the reticulo-endothelial and haemopoetic systems Nocturnal severe itch is a fairly constant finding in scabies, but is not entirely characteristic as most itchy skin diseases itch worst when the patient is warm in bed. Absence of itching is a diagnostic point in early syphilis but tabetics may itch intolerably

Pain is felt with inflammatory diseases such as boils and abscesses. Severe pain and tenderness is characteristic of tuberculous ulcer on the tongue, but a syphilitic gummatous ulcer in the same place is painless. Syphilitic chancres are usually painless, unlike the lesions of chancroid.

Hyperalgesia to the lightest touch is commonly found just before the rash of zoster appears and in the early days of the disease and pain follows later hyperalgesia is also a symptom of cutaneous myomas.

Anaesthesia and *analgesia*, which must be confirmed or discovered by test, are found in some cases of leprosy and in patients with skin disorders as a result of diseases of the nervous system.

The evolution of lesions may be suggestive of certain diseases such as chickenpox, smallpox, parapsoriasis guttata, etc. and

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lesions in crops is a characteristic feature of chickenpox and pityriasis rosea. Many diseases, whether usually generalized or not, have a particular predilection for certain skin areas. The common diseases of various skin areas are listed below

Scalp Tinea capitis (children particularly) alopecia areata, alopecia and other lesions of lupus erythematosus, lichen planus, pseudo-pelade, impetigo (often with pediculosis) psoriasis, seborrhoeic dermatitis.

Face Acne vulgaris, zoster herpes simplex, erysipelas, impetigo sycosis barbae, rosacea, lupus erythematosus, lupus vulgaris, gummas, seborrhoeic dermatitis, allergic contact dermatitis, pellagra and other lucites, basal-cell epithelioma and squamous-cell carcinoma, haemangioma, milia, xanthomas, molluscа contagiosa, fungous infections, warts

Lips Allergic, solar glandular and granulomatous cheilitis, urticaria, lupus erythematosus, herpes simplex, syphilis (early and late) lupus vulgaris, leukoplakia and squamous-cell carcinoma, perlèche.

Neck. Furuncles, carbuncles, sycosis nuchae, fungous infections, scrofuloderma, actinomycosis, contact dermatitis, pellagra.

Axillae Fungous infections, contact dermatitis, furuncles and chronic infections of apocrine glands, seborrhoeic dermatitis.

Trunk. Seborrhoeic dermatitis, acne, tinea versicolor pityriasis rosea, keloid, zoster morphoea, psoriasis, dermatitis herpetiformis, scabies urticaria.

Buttocks. Furuncles, scabies, acne conglobata, sandworm in children, napkin rashes.

Anal region. Pruritus ani from various causes, early syphilis, psoriasis, seborrhoeic dermatitis, warts, fungous infections.

Genitalia. Early syphilis and other venereal diseases, herpes simplex, warts, scabies, psoriasis, lichen planus, pruritus, contact dermatitis, lichen simplex chronicus, moniliasis, leukoplakia, squamous-cell carcinoma.

Groins Fungous infections, seborrhoeic dermatitis, pellagra, granuloma inguinale lymphogranuloma venereum.

Thighs Contact dermatitis, scabies, psoriasis, eczema.

Legs Lichen planus, psoriasis, prurigo nodularis, erythema nodosum, erythema induratum, varicose ulcers and eczema, late syphilis, Kaposi's sarcoma, insect bites, pellagra.

their *involution* to scars or pigmentation of diagnostic value in others such as tertiary syphilis, scleroderma, dermatitis herpetiformis or lupus erythematosus

The rate of spread or growth of lesions may help in differentiating clinically similar conditions e.g syphilitic gummas spread faster than lupus vulgaris and keratoacanthoma grows quicker than squamous-cell carcinoma.

Grouped lesions are characteristic of zoster and herpes febrilis, and originally solitary or grouped lesions followed by dissemination are seen in such conditions as impetigo syphilis and pityriasis rosea

The shape or configuration of lesions is sometimes of importance in psoriasis (serpiginous or geographical) secondary syphilis and lichen planus (circinate) erythema multiforme (target-shaped) tertiary syphilis (gyrate or serpiginous) zoster scleroderma and naevi (zoniform or band like) Koebner's phenomenon of linear distribution of lesions along scratch marks is seen in psoriasis, lichen planus and eczema.

The colour of lesions may be helpful (e g yellow in xanthoma ham-coloured in secondary syphilis) as also their *consistence* (cartilaginous infiltration below some chancres, stony hard below squamous-cell carcinoma) their *surface* (muscle-like in a syphilitic chancre covered with wash leather slough in a gummatous ulcer) and their *contents* or *secretions* (granules in the pus in actinomycosis)

Recurrence of lesions in situ is characteristic of allergic reactions to certain drugs (fixed eruption from sulphonamides, etc.) and herpes simplex.

Co-existing lymphadenopathy and the distribution and feel of the enlarged glands is of diagnostic value in early syphilis (painless and rubbery) squamous-cell carcinoma (stony hard) coccal and bacterial infections (pain and suppuration) lymphogranuloma venereum (chronic enlargement fistulae) and diseases of the lympho-reticular system

Distribution of lesions In some diseases the distribution of the lesions is such that the diagnosis is suggested even when the primary lesions have become unrecognizable through scratching infection or eczematization Such is the case in scabies psoriasis, pellagra, ichthyosis, atopic eczema, pityriasis rosea zoster and some of the infectious fevers The appearance of

excised under local anaesthesia care must be taken not to distort the area to be examined by injecting into it. The specimen should be as generous as possible considering the site from which it comes. A wide ellipse of skin, 1 cm. long, including the whole lesion if this is feasible, is the ideal minimum size. It is not always necessary to include normal skin but subcutaneous tissue should be excised where possible. Biopsy punches are preferred to the scalpel by some workers. Specimens should be lifted out with a hook rather than with forceps. The best fixative for ordinary use is fresh 10 per cent formalin. The pathologist must be told the site from which the specimen came and given clinical details of the case and differential diagnosis.

Serum tests are used in ordinary practice only for the diagnosis of syphilis, but have special applications in some virus and fungous diseases.

Wood's light is of great value in the diagnosis and follow up of cases of tinea capitis. It can also be used to demonstrate some skin lesions not apparent on examination in daylight.

Radiological examination is used in the diagnosis of sarcoidosis, tuberculosis, syphilis and other granulomatous diseases.

Patch testing is an essential part of the investigation of allergic contact dermatitis. This and passive transfer tests are discussed with the allergic diseases.

Percutaneous (scratch) and intracutaneous tests with allergens are sometimes used in allergic skin diseases, but their interpretation by the amateur is often difficult and their value questionable except in the case of inhalants.

Feet Fungous infections, contact dermatitis, scabies, warts, psoriasis, late syphilis, melanoma, sandworm

Hands Fungous infections and dermatophytides, contact dermatitis, erythema multiforme erysipeloid, granuloma annulare, warts, pellagra, syphilis, lucites, epidermolysis bullosa, solar and senile keratoses, squamous-cell carcinoma

Arms Contact dermatitis, atopic dermatitis psoriasis lichen planus erythema multiforme, scabies, warts, fungous infections, pellagra.

Buccal mucosa Syphilis, pemphigus erythema multiforme, pellagra, lichen planus leukoplakia, aphthae, moniliasis, allergic and infective stomatitis, squamous-cell carcinoma

AIDS TO DIAGNOSIS

Direct microscopical examination of the contents or secretions of lesions is of particular value in the diagnosis of early acquired or congenital syphilis where the living *Treponema pallidum* can usually be identified by dark-ground examination

Bacteria and fungi can be recognized in specimens of tissue and secretions, but precise identification usually rests on the results of culture. Sensitivity tests on cultured organisms may be of great value as a guide to the proper choice of antibiotics in the treatment of some infective diseases.

Inoculation of animals is used sometimes in the investigation of bacterial viral and fungous diseases.

Lepra bacilli can be identified in tissue scrapings in cases of lepromatous leprosy Tzanck popularized the method of examination of smears and scrapings, particularly of the floors of bullous lesions, by which diagnosis may be possible from the demonstration of pathological cell types The Tzanck test is of limited value and cannot be compared for specificity with proper histological examination after biopsy

Biopsy is the most important diagnostic aid in dermatology In most cases the specimen should be taken from a fully developed lesion, but sometimes it is necessary to examine early established and involuting lesions Early unbroken lesions are taken in the case of bullous eruptions. The skin is

excised under local anaesthesia care must be taken not to distort the area to be examined by injecting into it. The specimen should be as generous as possible considering the site from which it comes. A wide ellipse of skin, 1 cm. long, including the whole lesion if this is feasible, is the ideal minimum size. It is not always necessary to include normal skin, but subcutaneous tissue should be excised where possible. Biopsy punches are preferred to the scalpel by some workers. Specimens should be lifted out with a hook rather than with forceps. The best fixative for ordinary use is fresh 10 per cent formalin. The pathologist must be told the site from which the specimen came and given clinical details of the case and differential diagnosis.

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CHAPTER IV

PRINCIPLES OF TREATMENT

LOCAL TREATMENT

The human skin is a remarkably resilient organ. Treat the diseased skin gently and courteously and it usually responds by healing; treat it roughly or incorrectly and it rebels.

Accurate diagnosis must precede specific treatment. If the diagnosis is in doubt, treat symptomatically with simple remedies that will neither irritate nor obscure the view of the progress of the disease. Take as an example a young adult who presents with a round erythematous, scaling and perhaps vesicular lesion on the chest. All that is round is not ringworm; the lesion may be the herald patch of pityriasis rosea or a patch of infective or nummular eczema. An erroneous diagnosis of ringworm and the use of Whitfield's ointment may grossly inflame the lesions of pityriasis rosea or eczema. In such a case, if facilities for accurate diagnosis are lacking, use some mild fungicide such as a fatty acid if there is any doubt. On no account use gentian violet or any dyestuff; if a second opinion should be required the lesion will be unrecognizable.

Many patients who consult dermatologists are suffering from two diseases, the original and contact dermatitis caused by local medication prescribed by unwary practitioners, by pharmacists or the patient himself. I have long contended that dermatological practice would suffer severely if pharmacists were permitted to dispense only calamine lotion without a prescription. The commonest causes of contact dermatitis medicamentosa are preparations containing sulphonamides, penicillin, antihistaminics and local anaesthetics of the novocaine series. Such remedies should seldom, if ever, be used.

The diseases for which specifics are available present little difficulty in choice of remedy. It is in the treatment of chronic diseases such as atopic eczema and psoriasis that the amateur in dermatology will find that only experience and not the text

book, will tell him what to use at the different stages of evolution of the disease. If he sticks at first to the maxim that undertreatment does less harm than overtreatment, he and his patient will emerge triumphantly

The attentive student at dermatological clinics will note that although the dermatologist may have a large repertoire of prescriptions he uses only a very limited range of remedies in the local treatment of many of the common skin diseases Let him note these and use them largely until he feels confident of their value and indications before he embarks on wider range experiments. The prescriptions of the British Pharmacopoeia for the standard remedies such as calamine lotion and zinc cream are usually as good as, and cheaper than, proprietary equivalents. Experience and experiment will show in the wider field what proprietary remedies are more elegant and effective than the standard prescriptions.

Physical and mental rest and change of environment are sometimes just as important as actual medication, and here again only experience will teach how to select the patients who are best treated in their own homes and who should be admitted to hospital Unless nursing personnel trained in the treatment of skin diseases is available home is often better than hospital provided no elaborate investigations or treatment are indicated.

There are no set rules for the choice of local applications, but in general it is best to use baths, wet dressings and lotions in cases of acute and exudative dermatoses ointments are rarely indicated here and should never be first choice. In subacute states with little exudation lotions, emulsions or pastes may be used. Ointments are used for non-exudative conditions.

Cleansing of the skin may be a necessary preliminary to treatment, and the patient should be told what he may or may not use before and during treatment and at varying stages of his disease. Many patients will tell the dermatologist that they have long been forbidden the use of soap and water Soap may well often irritate existing dermatoses and cause some, but water alone is not often contraindicated provided maceration of the skin by prolonged bathing is avoided and drying is gently accomplished. When soap is permitted, let it be a toilet soap medicated soaps have no intrinsic merit and may even

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be applied with a soft flat brush or cotton wool. Remember in prescribing that eight ounces of lotion are required to cover the whole body surface. When expensive hydrocortisone lotions are prescribed for small areas, instruct the patient to spread them with clean fingers for greatest economy.

It is not necessary to be eternally cleaning lotions off before applying the next dose: cleanse when necessary, otherwise add.

Creams, liniments and emulsions are easily-spread, oil and water combinations containing varying amounts of the principal ingredients with emulsifying agents to keep the compound stable. Powders such as calamine and zinc oxide may be added and medicaments incorporated as in lotions or ointments. Zinc cream and calamine liniment are commonly used members of this group. They are used particularly for widespread lesions when exudation is minimal and some emollient action is required.

Pastes are semi-solid suspensions of insoluble powders in greasy bases. They possess a little absorbent power and may be used even on lesions producing a little exudate. Medicaments may be incorporated. Lassar's paste (paste of zinc oxide and salicylic acid, B P) is much used and to it may be added coal tar, chrysarobin, etc. Pastes are spread on fairly thick and added to when necessary: frequent cleaning is undesirable and pastes are often used in the manner of a splint to protect the skin.

Ointments are greasy bases incorporating various medicaments. They are seldom used on exudative lesions which they generally irritate and cause to exude even more serum. They are not well tolerated on hairy skin apart from the scalp or on the warm, moist skin folds such as the natal cleft or axillae. The ointment bases most commonly used are soft paraffin and lanolin, but in many circumstances bases incorporating emulsifying agents, such as Unguentum emulsificans B P., are more convenient in that they are more penetrating, easier to remove and may be diluted with water and adapted to incorporate water-soluble but oil insoluble substances.

The patient should be instructed to massage a minimum quantity of ointment into the skin and then wipe away all excess. In many circumstances too much of the correct ointment will have the paradoxical effect of making the

cause sensitization In some conditions where soap is contra indicated a detergent may be tolerated and permissible proprietary preparations of liquids and cakes are available When both soap and detergents are inadvisable or not tolerated oatmeal is a satisfactory non irritating substitute it is used in a muslin bag or an old sock as is a sponge, the water being expressed on the skin

Bathing in potassium permanganate solution is useful for cleansing for softening scabs and crusts on large areas and for the treatment of some exudative diseases. For an ordinary bath half a teaspoonful of the crystals is required this should previously be dissolved in a jug of water and not thrown into the bath as the crystals melt slowly Smaller areas may be cleaned or treated with frequently changed linen or cotton cloths soaked in a 1 10 000 solution of potassium permanganate

Very adherent scabs and crusts as on the scalp may be removed by starch poultices or by soaking in mineral or vegetable oil Routine cleansing of the scalp when ointments are in use is best performed with a detergent shampoo

Powders are used particularly for treating intertrigo of the great skin folds Their action is mainly one of drying and reducing friction, but medicaments may be added Medicated powders have a place in treatment and in prophylaxis of fungous infections of skin folds Proprietary powders are preferred

A patient suffering from a widespread dermatosis, such as pemphigus with moist and eroded lesions which are irritated and aggravated by dressings may be nursed naked between sheets in a bed of talcum powder

Lotions are liquid preparations containing medicaments in solution or suspension No great absorption of included medicaments is to be expected when they are incorporated in lotions. The commonest and most useful lotion is calamine lotion that of the British Pharmacopoeia contains 0 5 per cent phenol but one containing 2 per cent gives a better anti pruritic effect. To basic calamine lotion may also be added 1 to 5 per cent of ichthammol, which has a mild antiseptic and soothing effect, or 2 to 5 per cent of precipitated sulphur which is useful in the acute phases of seborrhoeic dermatitis. Lotions are especially useful in widespread dermatoses and may here

Compound tar ointment

Solution of coal tar	12.5
Ammoniated mercury	5
Salicylic acid	5
Emulsifying ointment B.P. to make	100

Whitfield's ointment

Benzoic acid	5
Salicylic acid	3
Soft paraffin	25
Coconut oil to make	100

Sulphur and salicylic acid ointment

Precipitated sulphur	2
Salicylic acid	2
Benzoated lard	25
Coconut oil to make	100

Lassar paste

Salicylic acid	2
Zinc oxide	25
Starch powder	25
Soft paraffin to make	100

Sulphur and resorcin paste

Resorcin	6
Sulphur	6
Zinc oxide	38
Soft paraffin to make	100

Dales paste

Sulphur	15
Zinc oxide	15
Coal tar	15
Soft paraffin to make	100

CORTICOSTEROIDS AND ACTH

The pituitary adrenocorticotrophic hormone (ACTH) controls the production of hormones by the adrenal cortex. The adrenal hormones used in dermatological practice are the glucocorticoids, cortisone or hydrocortisone like hormones, which have anti-inflammatory and antiallergic effects. Apart

condition worse by causing maceration Only when an ointment is used for softening some hard lesion should it be liberally applied

The majority of skin diseases heal best if left exposed and there is almost no place for occlusive dressings or heavy bandages and cotton wool To avoid friction and staining of clothing use old cotton or linen cloth or butter muslin lint and gauze stick to and irritate moist lesions Ambulant patients with widespread lesions may wear light cotton pyjamas under their clothing

PRESCRIPTIONS

Castellani s paint

Saturated solution of basic fuchsin	10
Aqueous solution of phenol, 5 per cent	100
Filter and add boric acid	1
After two hours add acetone	5
After two hours add resorcin	5

Scalp lotion

Mercury perchloride	0·2
Resorcin	1·0
Castor oil	2·0
Alcohol 60 per cent to make	100

L eau Dalibour

Copper sulphate	1
Zinc sulphate	1 5
Camphor water to make	100

Lotio alba

Precipitated sulphur	3
Zinc sulphate	3
Sulphurated potash	3
Rose water to make	100

Phenol and menthol ointment

Phenol	1
Methol	2
Zinc oxide	6
Emulsifying ointment B.P to make	100

Compound tar ointment

Solution of coal tar	12.5
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Emulsifying ointment B.P. to make	100

Whitfield's ointment

Benzoic acid	5
Salicylic acid	3
Soft paraffin	25
Coconut oil to make	100

Sulphur and salicylic acid ointment

Precipitated sulphur	2
Salicylic acid	2
Benzoated lard	25
Coconut oil to make	100

Lassar's paste

Salicylic acid	2
Zinc oxide	25
Starch powder	25
Soft paraffin to make	100

Sulphur and resorcin paste

Resorcin	6
Sulphur	6
Zinc oxide	38
Soft paraffin to make	100

Dale's paste

Sulphur	15
Zinc oxide	15
Coal tar	15
Soft paraffin to make	100

CORTICOSTEROIDS AND ACTH

The pituitary adrenocorticotrophic hormone (ACTH) controls the production of hormones by the adrenal cortex. The adrenal hormones used in dermatological practice are the glucocorticoids, cortisone or hydrocortisone-like hormones, which have anti-inflammatory and antiallergic effects. Apart

from cortisone and hydrocortisone there are available for clinical use synthetic derivatives of these hormones which have greater anti inflammatory action but less side-effects as regards salt retention among these are prednisone, prednisolone methylprednisolone, triamcinolone and dexamethasone which are marketed under a variety of trade names.

ACTH is used less in clinical medicine than are the adrenal steroid hormones and some would have it that there is little place for it at all There are cases and conditions however in which it acts better or more quickly than steroid hormones and cases where it is effective when the steroids are ineffective Occasionally there are encountered cases requiring prolonged treatment which react best at certain times to steroid hormones and at others to ACTH so that one must change about according to reaction Patients requiring prolonged steroid hormone treatment at high dosage levels should be given a weekly dose of ACTH (40 units of the gel) to stimulate adrenal cortical secretion of the natural hormones which otherwise tends to diminish.

When rapid action is necessary ACTH should be ad ministered intramuscularly in aqueous solution at the rate of 25 units or more every six hours As improvement occurs the dosage is reduced gradually every few days to 20 15 10 units six hourly and then to eight hourly dosage, twelve hourly then daily Always taper off slowly to avoid rebound effect though the rate of tapering will vary according to circumstance

In less acute conditions where ACTH proves superior to steroid hormones or for prolonged treatment of chronic conditions the slow acting ACTH gel may be used The starting dose may be 80 units daily and the maintenance dose 40 units daily In tapering off reduce dose and increase spacing Some preparations are reputed to give effect for forty-eight hours between injections be wary of such long spacing at the start of treatment.

The type of steroid hormone to be used in dermatological conditions is a matter for individual choice and experience For diseases requiring only short term treatment cortisone is satisfactory and cheaper than the other preparations The starting dose is again gauged by experience but it will vary between a total of 100 and 300 mg given in four divided doses

per day The total daily dose is gradually reduced and tapered slowly off In some cases tapering off can only very gradually be achieved by reducing the average daily dose by 12 5 mg at weekly intervals. In chronic diseases, experiment determines the correct maintenance dosage which usually varies between 37 5 and 100 mg. daily Whatever the total dose it works best when divided over four doses daily

When hydrocortisone is used the starting total dose is between 80 and 240 mg daily and maintenance dosage is 30 to 80 mg

Prednisone and prednisolone are, weight for weight, more potent than cortisone loading dosage is 20 to 60 mg daily maintenance dosage 5 to 20 mg

Triamcinolone or methylprednisolone are used in loading dosage of 12 to 20 mg daily and maintenance dosage of 2 to 4 mg daily The loading dose of dexamethasone is 2 4 to 4 mg daily the maintenance dose 0 4 to 0·8 mg These preparations, in the dosage range commonly required for the treatment of skin diseases, are much less liable than their predecessors to cause minor side-effects such as salt retention and euphoria.

Injectable steroid hormone preparations for intravenous use are of the greatest value in the treatment of emergencies such as anaphylactoid reactions and laryngeal oedema.

The main contraindications to corticosteroid and ACTH therapy are diabetes, severe hypertension, bleeding states, psychiatric disturbances, active or latent tuberculosis and peptic ulcer

Side-effects of treatment, usually reversible, are mainly those of a spontaneous Cushingoid syndrome with weight increase from salt and water retention, hypertension, oedema of the face ("moon face") and extremities, striae, hirsutism in women, acneiform eruptions, purpura and glycosuria. Mental changes of varying type and severity are encountered wakefulness and mild euphoria are fairly common Osteoporosis with fractures of vertebrae may occur Allergic reactions to traces of animal proteins in ACTH occur rarely

These complications are seldom seen in the treatment of acute dermatological conditions and when they occur in chronic conditions where steroid therapy is essential the milder

ones may have to be ignored or treated by change of remedy or dosage rather than by withdrawal

It must always be remembered that ACTH and cortisone never cure diseases but only suppress symptoms. They are not to be used as a disguise for ignorance in undiagnosed diseases Patients on long term treatment must be examined weekly their blood pressure recorded and urine tested for sugar

The absolute indications for systemic ACTH or steroid hormone therapy are few Life is prolonged by their use in *pemphigus systemic lupus erythematosus* and *systemic periarteritis nodosa*. In the last two diseases treatment should not be started unless the condition warrants it once started it may never be possible to discontinue it and many cases fluctuate spontaneously at a non lethal level for a very long time. *Dermatomyositis* deserves treatment though the results may sometimes be equivocal Some cases of rapidly progressive *scleroderma* may be benefited but results are seldom brilliant. *Exfoliative dermatitis* of allergic origin usually responds rapidly to treatment that due to diseases of the reticulo-endothelial or haemopoietic systems may be temporarily alleviated Cortico-steroids plus antibiotics may be remarkably effective in *postoperative progressive bacterial synergistic gangrene*

The occasional indications for systemic therapy are numerous, but care must be taken in the selection of cases.

Erythema multiforme Severe cases of all types deserve treatment and usually respond in spectacular fashion Aqueous solution of ACTH is recommended at the outset

Contact dermatitis Very effective, but to be used only for very severe and extensive cases, preferably after the cause has been identified

Drug eruptions Usually effective to be reserved for severe cases.

Urticaria Use only for very acute urticaria or angio-neurotic oedema Steroid hormones are best Intravenous therapy is used in emergency Results in chronic urticaria are no better than with other remedies.

Atopic dermatitis Steroid hormones may be used for the very severe episodes that punctuate the course of some cases of atopic dermatitis Chronic, very severe cases may require prolonged suppressive treatment provided the maintenance

dose is reasonably low this is not dangerous. Think very carefully of the consequences, financial and otherwise, before using ACTH or steroids in atopic dermatitis.

Seborrhoeic dermatitis In rare cases of severe, generalized seborrhoeic dermatitis only ACTH or cortisone give relief. They are never the first choice Protracted courses may be necessary to suppress the disease

Nummular eczema ACTH or cortisone may be necessary for severe, widespread chronic cases resistant to all other treatment. Results are sometimes enhanced when antibiotics are used simultaneously

Allergides ACTH and steroid hormones have been tried in many of the proven or suspected microbic allergides. Temporary suppression of symptoms is usually all that results. This type of treatment is sometimes justified in very severe epidermophytide reactions, but in diseases such as nodular dermal allergides or purpura pigmentosa progressiva it is pointless.

Erythema nodosum. Steroid hormone therapy is sometimes the only effective remedy here, but before using it one must naturally be satisfied that the basic cause of the disease is not one such as tuberculosis or coccidioidomycosis which could be flared up thereby

Sarcoidosis Temporary improvement is fairly common, lasting improvement is rare and cure is not to be expected. There are considerable variations in response in different cases to the different remedies, but ACTH is generally better than steroid hormones. Such treatment is definitely indicated for trial in cases with important symptoms due to pressure by enlarged glands on mediastinal structures.

Lichen planus ACTH and steroid hormones are of little or no value in the treatment of the ordinary varieties of lichen planus where temporary alleviation in a small percentage of cases is all that can be expected. They are worthy of trial, however in cases of pseudo-pelade in which lichen planus is the cause (ACTH is first choice here) and in acute disseminated cases seen very early in the disease. Lichen planus-like drug eruptions react quickly to treatment.

Psoriasis Steroid hormone or ACTH therapy may cause remarkably rapid regression of lesions in some cases of psoriasis,

but sudden suspension of treatment is almost invariably followed by a rebound phenomenon in which the relapse lesions are worse than those of the original attack. Until recently it was the general rule to use these remedies only for severe arthropathic psoriasis Experiments have been resumed since the advent of the relatively non toxic triamcinolone and methylprednisolone. These may be tried in severe and resistant cases of ordinary psoriasis and sometimes give very good immediate results.

Dermatitis herpetiformis Rare cases of dermatitis herpetiformis and allied bullous diseases resist all forms of treatment except cortisone or ACTH These remedies are never the first to be used

In the case of the diseases just reviewed under occasional indications it should be the aim when the condition is a chronic one, to use ACTH or steroid hormones as emergency treatment to bring the disease down to a level of activity where simpler remedies may take effect.

The list of skin diseases in which steroid hormones have been used without success may be said to include all other diseases not already mentioned some deserve mention Although the effects in systemic lupus erythematosus are spectacular chronic discoid lupus erythematosus does not react at all Keloids are unaffected by systemic treatment or by local injections or inunctions

It would be unwise at present to be too dogmatic about the use of ACTH and steroid hormones their fields of activity may yet be widened and thoughtful experimentation is quite justified

Local therapy Cortisone has no effect but hydrocortisone and some other steroids are potent anti inflammatory agents when applied to the skin They are available as lotions or ointments and expense is the main limitation to their use Lotions are more economical than ointments, but are not always so effective. Side effects are rare but salt retention and oedema are reported in cases lavishly treated with fluorohydrocortisone

Local therapy is indicated for diseases affecting relatively small areas. The preparations marketed at present contain between 0 5 and 2 5 per cent of the active principle the difference in effect is not as one is to five at the two ends of the scale

and personal experience is that the one is as good as the other Pressure spray solutions designed for treating large surfaces are available in cases where such steroid therapy might be indicated it will be found that systemic treatment is more effective and much cheaper

Conditions in which lotions or ointments are usually very effective include allergic contact dermatitis, ano-genital pruritus and localized eczemas of other varieties. In chronic conditions such as infantile and atopic eczema they should be reserved for use in exacerbations.

When the above conditions are complicated by secondary infection, combined local antibiotic and steroid hormone therapy will give the best results. Such combinations are marketed, the antibiotic most commonly employed being neomycin.

Combined therapy is also of value in some cases of chronic infective dermatoses such as pityriasis streptogenes, otitis externa, sycodermatitis perstans and nummular eczema.

Contact sensitization to such preparations is rare, so that there is no bar to reasonable experiments with local steroid hormone therapy plain or with antibiotics. Let it be remembered however that there are cheaper antipruritics available for diseases where the steroid hormones may palliate but have no hope of curing

THE ANTIMALARIALS

The modern antimalarial remedies have been widely used in dermatological practice since 1951 when Page published an article on the use of Mepacrine in chronic discoid lupus erythematosus. Page was not the first in this field but his work was the first to attract general attention

Quinacrine (Atabrine, Atebrine, Mepacrine) is an acridine derivative which, when administered orally for prolonged periods, has a marked effect in suppressing the lesions of chronic discoid lupus erythematosus. It may also be effective in other dermatoses in which photosensitivity is an important factor Although it is no longer widely used in dermatology other antimalarials having taken its place, there are occasional cases in which it is the most effective remedy

The dosage for an adult with chronic lupus erythematosus is 100 mg orally thrice daily until the skin begins to show a

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very occasionally make it necessary to suspend treatment. Patients unable to tolerate Nivaquine or Aralen may be able to use Plaquenil.

Th dosage suggested above may be used for other lucites with varying degrees of success. In polymorphic light eruptions, pellagroid dermatoses and acute lucites generally good results are anticipated, but in cutaneous porphyria results are poor and it is doubtful whether one is justified in using chloroquine which has been reported to precipitate attacks of acute porphyria.

Results in chronic solar dermatoses are harder to assess, but chloroquine is safe enough to prescribe in any case where it might be of value A minimum trial of three months is necessary to decide whether to persist or to desist. Early solar cheilitis may be obviously benefited so too, may be cases of multiple solar keratoses. Good results are reported in cases of xeroderma pigmentosum. Solar sensitivity may be reduced and life made more comfortable for albinos and patients with widespread vitiligo of exposed skin

The exact mode of action of the antimalarials is not clear and it may well be more than a mere filtering or blocking effect on the sun s rays. Antimalarials are used apart from the lucites with occasional reported success in systemic lupus erythematosus, rheumatoid arthritis, dermatitis herpetiformis and, with aureomycin, in pemphigus. Other applications may well be found

THE ANTIBIOTICS

Antibiotics, both systemically and locally applied are of great value n the treatment of microbic infections of the skin. In many cases the appropriate antibiotic can be selected as a result of experience, in others identification of the organism and investigation of its sensitivity towards the various antibiotics may be necessary These matters are discussed in the text.

Penicillin is still the most used and probably the most useful antibiotic but it has the major drawback of frequently causing reactions from sensitization. It should never be used for local application, and before it is given systemically the patient must be interrogated about previous penicillin medica t on and any reactions thereafter Systemic penicillin is often

yellow tinge (2 to 4 weeks) then 100 mg twice daily for a month then 100 mg daily until maximum clinical improvement is attained Thereafter dosage is gradually reduced until it can be suspended or until maintenance level is calculated

A major drawback to quinacrine is the obvious yellowing of the skin that it produces. This fades slowly when treatment ceases but traces may remain for many months even for a year or two In cases treated for six months or more there may appear a dusky blue discoloration of the nail beds and, less often of the hard palate and cartilaginous structures of the nose and ears

Toxic effects are fairly common Eczematous dermatitis, patchy or widespread exfoliative dermatitis and lichen planus-like dermatitis may occur The last may be very extensive and almost always affects the buccal mucosa it is clinically and histologically indistinguishable from spontaneously-occurring lichen planus, but is susceptible to treatment with ACTH and corticosteroids. Malaise fever gastro-intestinal upsets, psychoses, hepatitis, visual disturbance and leukopenia are other hazards.

Chloroquine It was soon found that other antimalarials worked as well as quinacrine in the light-sensitivity diseases, *did not discolour the skin and caused much less trouble from* side-effects. The drugs most used are 4-amino-quinolines (chloroquine, Aralen Nivaquine, Plaquenil) In chronic lupus erythematosus a satisfactory schedule in most cases is 200 mg orally thrice daily for the first week, 200 mg twice daily for the second week and 200 mg once daily thereafter until symptoms have subsided as far as they will Further reductions are then made until treatment is suspended or maintenance dosage determined Maintenance dosage may vary from season to season some patients who need protection in summer may be able to suspend treatment in winter

Major toxic effects occur exceptionally rarely lichenoid skin eruptions may occur after prolonged treatment and bleaching of the hair is reported A common mild phenomenon is gastric irritation, especially when two or three daily doses are being taken suspend treatment until symptoms cease, then resume with one 200 mg dose daily and no further trouble is likely to arise. Anorexia loss of weight and depression may

this is not always so chronic urticaria is less responsive than is the acute form

They are useful antipruritic agents and may give symptomatic relief in many itching dermatoses. Drowsiness is a side effect of treatment that is not unwelcome in some cases.

Side-effects from systemic antihistaminics occur fairly frequently but are seldom of major concern. They include depression or more rarely stimulation of the central nervous system, gastro-intestinal disturbances, dryness and metallic taste in the mouth frequency of urination and palpitations. Dermatitis occurs infrequently it may begin on exposed skin. Leukopenia and agranulocytosis very rarely occur

Benadryl and Phenergan are probably the most potent antihistaminics, but both are very liable to cause drowsiness and may not be acceptable to the ambulant patient. Benadryl is given in 50 mg doses, 3 or 4 times daily Phenergan is given in 10 mg doses, 3 or 4 times daily or in a single nocturnal dose of 25 mg Elixirs are available for children.

There are too many other preparations to mention all of them. They are generally less potent than Benadryl and Phenergan, but some are less liable to cause unpleasant side effects and are thus more useful for the out patient. Every dermatologist has his own favourites mine are Anthisan Chlor Trimeton and Sandosten.

Slow release preparations with prolonged action are also available they seem to me no better than Phenergan. Injectable preparations may be used in emergency but in an emergency the steroid hormones would be preferable

SEDATIVES

Relief of anxiety and tension as well as of itch is of paramount importance in some patients with skin diseases. The more depressing antihistaminics may be useful in such cases as may be the common aspirin. Luminal is seldom of much value to adults, but children may benefit from it. Useful soporifics are Soneryl and Seconal.

In vogue at present are the tranquillizers which soothe without causing drowsiness Chlorpromazine (Largactil) is much prescribed in doses of 25 to 50 mg 3 or 4 times daily It has the drawback of causing side effects such as jaundice and

followed by urticaria which must be quickly and energetically treated some cases become extremely chronic and intractable if they are originally ignored Severe and even fatal anaphylactoid reactions may occur Penicillinase, which quickly neutralizes penicillin promises to be valuable for treating allergic reactions

Streptomycin is so potent a contact sensitizer that it must never be used on the skin this fact is, fortunately recognized by the manufacturers The main sufferers are nurses who inject streptomycin Systemic streptomycin is of the greatest value for tuberculosis of the skin as of other organs but it may cause a variety of allergic reactions ranging up to exfoliative dermatitis.

The best general purpose antibiotics for local treatment of the common superficial infective dermatoses are aureomycin and neomycin. Neither is commonly productive of contact allergic reactions In certain circumstances combinations of an antibiotic and hydrocortisone or fluorohydrocortisone in lotion or ointment forms are more effective than either component alone

THE SULPHONAMIDES

Sulphonamides should on no account be used in local applications to the skin as the danger of sensitization is much too great. Systemic sulphonamides have little value in dermatology except in dermatitis herpetiformis where sulphapyridine is sometimes a useful suppressive agent.

THE ANTIHISTAMINICS

The antihistaminics antagonize many of the pharmacological actions of histamine They have a specific effect only in urticaria and seasonal hayfever elsewhere any palliative effects they exercise are nonspecific. They protect animals from fatal anaphylactic reactions

Antihistaminics are so prone to cause allergic contact dermatitis that their use in ointments and lotions is absolutely contraindicated

Systemic antihistaminics are indicated in urticaria Theoretically they should control any urticaria, but in practice

this is not always so chronic urticaria is less responsive than is the acute form.

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photosensitivity Nurses who administer it by injection frequently develop allergic contact dermatitis and recurrences may be provoked even by handling the pills

Reserpine (Serpasil) an alkaloid extracted from *Rauwolfia serpentina* is a satisfactory tranquillizer with negligible tendency to produce major side-effects The dosage required to give relaxation varies from patient to patient. Some do well on 0 1 mg thrice daily others need 0 25 mg thrice daily Drowsiness is often noticed in the first few days if dosage is begun at thrice daily level. This is avoided by giving one tablet daily for three days, two daily for three days then three daily The good effects are not produced immediately but only after a few days Children tolerate the drug well

Meprobamate also deserves mention. Dosage begins with one 400 mg tablet at night for three days, then one tablet twice daily Dermatitis and other side-effects are reported.

X RAY THERAPY

X rays exercise an inhibitory effect on cellular activity and *this effect is most marked against rapidly-growing tissues* such as those of malignant growths In suitable dosage the x rays reduce pruritus diminish secretion in sweat and sebaceous glands, exercise a certain bactericidal action and cause cessation of cellular division and cellular death These properties would suggest that x ray therapy might have a very wide application in the treatment of dermatoses and this is, indeed, the view of many dermatologists and radiotherapists

The dangers of overdosage with x rays are well known and there is little divergence of opinion concerning the amount which can safely be given in a single dose without immediate ill effects The position is not so clear in relation to the amount which may safely be given in fractional doses, the method commonly used for dermatological conditions without fear of late atrophic and degenerative changes Some authorities consider a total dose of 1000r as safe others do not exceed 500r *Late effects* may appear only decades after treatment and nobody has yet followed a large enough series of treated patients for long enough to give a satisfactory answer to this question In prescribing x rays it is important therefore to

be convinced that they are entirely justified and to ensure that they are properly administered.

There are few cases in which x ray therapy is the only possible method that will effect a cure but there are some conditions in which it may be the treatment of election. This is so in cases of basal-cell epithelioma or squamous-cell carcinoma which because of size, situation or other considerations are unsuitable for surgical removal. For small, accessible tumours of this nature diathermy or excision are much simpler and less time-consuming than x-ray therapy and the results are equally good excision will be chosen if the cosmetic result is of major importance. Atrophy of some degree, possibly progressive atrophy must be expected after x-ray therapy for tumours. X-ray atrophy is to all intents and purposes identical with that seen in the chronic solar dermatoses and x ray therapy is, therefore seldom the treatment of election for patients with tumours supervening on such a basis the age of the patient will naturally be a consideration here

X ray therapy is useful to give temporary improvement in some diseases of the reticulo-endothelial and haemopoietic systems. It has little effect on the majority of benign skin tumours and none whatever on moles. Haemangiomas of the type naevus vasculosus (strawberry mark) are often radiosensitive but the best results are usually obtained by doing nothing at all.

Temporary epilation may be procured by x ray therapy and, until recently this was standard practice in the treatment of some varieties of tinea capitis. Preliminary studies suggest that treatment with the antifungous antibiotic, griseofulvin, may make epilation unnecessary

Beyond these limits there are no absolute indications for radiotherapy but there are some conditions where it may be employed with some reasonable expectation of success. Lichen simplex chronicus, where other means have failed is probably the most important of these. Another is chronic eczema persisting long after the apparent cause a contact allergen, has been removed In other varieties of eczema the effects of x-ray therapy are unpredictable and any improvement is usually temporary It is pointless to use radiotherapy as a

palliative in allergic dermatitis before the cause has been identified in infective dermatitis or in atopic eczema

In herpes febrilis which recurs frequently on the same site x ray therapy may bring long periods of relief No other virus disease is liable consistently or even frequently to benefit but radiotherapy is still much used for warts Provided the patient is a child and on the verge of spontaneous cure, the results may be satisfactory Radiotherapy is the last resort for isolated plantar warts mosaic warts should not be so treated The penalty for overdosage of a plantar wart is a chronic necrotic ulcer This is commoner than the radiotherapists would have us believe consult the plastic surgeon for statistics

Psoriasis is frequently but only temporarily improved or effaced by x ray therapy In a recurrent disease of this nature it is best never even to begin using x rays as the dangers of overtreatment are great if the effects are good and the patient stupid

Acne is another common disease often treated with x rays. Any improvement is likely to be temporary and the dosage required to obtain it is often beyond the safety level

The bactericidal action of x rays is so limited compared to that of other antibacterial agents that their use is not worthwhile in infective conditions Fungous infections are uninfluenced

X ray therapy is absolutely contraindicated in diseases such as lupus erythematosus where photosensitivity plays a part carcinoma complicating lupus erythematosus occurs almost always in cases so treated Permanent epilation or suppression of sweat or sebaceous gland secretion can be procured only at the expense of serious damage to the skin

Radium and radon therapy are used for malignant tumours of the buccal cavity and lips which are inaccessible to x ray therapy

Thorium X is a radioactive substance which emits alpha rays of limited penetrating power It is applied to the skin in an alcoholic solution or varnish Thorium X enjoys vogues of popularity when it is used for haemangiomas and alopecia areata which heal spontaneously ringworm of the nails which is uninfluenced by radioactive emanations and so forth

ULTRAVIOLET RAY THERAPY

Ultraviolet ray therapy is no longer in vogue and is, in any event, of very limited value in dermatological conditions. Finsen therapy was of great importance in the treatment of lupus vulgaris, but it has been superseded by the modern anti-tuberculous remedies. Ultraviolet irradiation is still sometimes used in acne and psoriasis and by enthusiasts, for a number of other conditions. In any disease where ultraviolet therapy is likely to help natural sunlight is more effective. It is dangerous in any condition such as lupus erythematosus, where photosensitivity is a causative factor

CARBON DIOXIDE ICE

Solid carbon dioxide may be used for the destruction by frostbite necrosis of small benign skin tumours. Snow can be prepared by allowing the compressed gas to escape rapidly from the cylinder through a special tiny jet into a chamois leather bag, or by using a Sparklet apparatus designed for the purpose and employing cartridges containing the gas. The snow is tamped into ice in a wooden or vulcanite tube of a diameter suited to the occasion If an icecream shop is nearby it is easier to obtain a block of "dry ice" and cut off convenient portions.

In treating a wart, for example a rod of ice of equal base diameter is firmly pressed on the lesion for so long as is necessary to produce a thin white rim of freezing in the surrounding skin. A bulla may form under the wart, which can then be snipped off, or more gradual degeneration may occur Diathermy is really a much neater method of dealing with small tumours.

Before the antimalarial drugs were used for chronic discoid lupus erythematosus freezing was a popular method of treatment. Today it is seldom required, but it may be useful for stubborn verrucous lesions persisting in spite of internal medication The ice is applied firmly for thirty seconds in the first instance but it will be found that thick lesions will take up to ninety seconds. The aim is to produce subsequent erythema and swelling, but to stop short of bulla formation Treatments are given once weekly

Strawberry haemangiomas are reputed to respond to this type of treatment my experience has been disappointing and I now rely on time alone to produce a cure

Freezing is the treatment of election in many cases of sandworm infestation A circle about 2 cm in diameter is frozen white at firm pressure one minute is required for lesions in thin epidermis two minutes for those on the palms or soles.

Surgical diathermy

Monopolar electrodesiccation is an extremely useful procedure for the removal of small skin tumours. Convenient portable machines such as the Hyfrecator are inexpensive and all that are required for consulting room operations This type of diathermy has largely superseded the galvanocautery and electrolysis whose effects it can reproduce or better Destruction of tissue is accomplished by sparking from suitably sized and shaped needles

The gauge setting of the machine must be adjusted each time it is used since it varies according to the type of needle and the lesion to be treated The operator must test against the skin of his palm raising the setting until a smooth spark is obtained This suffices for the preliminary delineatory cutting but a juicier spark may be required later for deeper tissues and to control bleeding points.

For tiny lesions no anaesthesia is required and in certain situations, such as the nose the pain of the sparking is much less than that produced by an injection The patient must be warned to expect some pain Only experience will tell how far one may go without anaesthesia A dental cartridge syringe with the finest needles is the best apparatus to use for minor dermatological surgery The site is prepared with surgical spirit and this must be allowed to dry before the diathermy is used, otherwise it flames up and causes alarm if not danger Ether should be avoided as a cleaning agent If insulation is faulty there may be heating of the skin where the operator rests his hand while working this is dangerous as it may cause the patient to start.

Here are the procedures to be used in treating some of the commonest conditions in which diathermy is useful

Warts It is pointless to try to remove by diathermy multiple common warts in children which in any event will disappear spontaneously Adults or older children with a few chronic warts may be so treated and local anaesthesia is usually advisable Insert the needle into the wart and switch on. The small wart lights up within, swells, seems to boil internally and becomes bullous When this occurs, snip off the boiled tissue with scissors or wipe away with gauze. Burn and wipe away the protruding base to just below skin level, then remove all charred remains and spark any bleeding points. Large warts require a few vertical and horizontal insertions of the needle before they are sufficiently cooked for the initial snipping off of the major part of the tumour Sparking may cease if blood or tissue coagulates on the needle wipe away and start again.

Healing is slow and proceeds best without dressings. If a dressing is required let it be light and not occlusive. Sealing in with adhesive bandages delays healing Warn the patient that a fortnight or more may pass before healing is complete

Multiple plane warts that resist simple methods are quickly sparked without anaesthesia. Take care not to destroy too deeply or scars may remain.

Filiform warts of the beard area in men should be treated by diathermy See the patient every fortnight and treat seedling warts as they arise This type of wart is extremely hard to eradicate but persevere

Genital warts, condylomata acuminata, should be treated with diathermy if podophyllum resin fails to cure them.

Diathermy is not the first line of attack for plantar warts except for the few which are prominent and *not on pressure* points.

Seborrhoeic warts basal-cell papillomas, are extremely easily removed with the diathermy With a vigorous spark run the needle here and there over the surface until the lesion becomes greyish and of gummy consistency Wipe off with gauze and spark any remains before finally cleaning the surface. More protuberant lesions can be transfixed and sparked. Destruction of tissue below surface level is unnecessary No dressing need be applied

Strawberry haemangiomas are reputed to respond to this type of treatment my experience has been disappointing and I now rely on time alone to produce a cure

Freezing is the treatment of election in many cases of sandworm infestation A circle about 2 cm in diameter is frozen white at firm pressure one minute is required for lesions in thin epidermis, two minutes for those on the palms or soles

SURGICAL DIATHERMY

Monopolar electrodesiccation is an extremely useful procedure for the removal of small skin tumours. Convenient portable machines such as the Hyfrecator are inexpensive and all that are required for consulting room operations This type of diathermy has largely superseded the galvanocautery and electrolysis whose effects it can reproduce or better Destruction of tissue is accomplished by sparking from suitably sized and shaped needles

The gauge setting of the machine must be adjusted each time it is used since it varies according to the type of needle and the lesion to be treated The operator must test against the skin of his palm raising the setting until a smooth spark is obtained This suffices for the preliminary delineatory cutting but a juicier spark may be required later for deeper tissues and to control bleeding points.

For tiny lesions no anaesthesia is required and in certain situations, such as the nose, the pain of the sparking is much less than that produced by an injection The patient must be warned to expect some pain. Only experience will tell how far one may go without anaesthesia A dental cartridge syringe with the finest needles is the best apparatus to use for minor dermatological surgery The site is prepared with surgical spirit and this must be allowed to dry before the diathermy is used otherwise it flames up and causes alarm if not danger Ether should be avoided as a cleaning agent If insulation is faulty there may be heating of the skin where the operator rests his hand while working this is dangerous as it may cause the patient to start.

Here are the procedures to be used in treating some of the commonest conditions in which *diathermy is useful*

the limbs will be seen to require treatment as well Repeated treatment will be required for multiple telangiectases of the nose or cheeks as the blanching eventually occludes the view This procedure is impossible under local anaesthesia

After-care. Healing after diathermy destruction of skin is always slow and the patient must be warned of this. He should be counselled against applying any dressing unless this is essential to avoid contamination at work. He should be told to wash just as usual, but to avoid maceration by water Women should obviously not apply cosmetic cream to treated areas on the face, but I have never seen harm come from a little concealment by powder once healing has started.

Infection of major degree is uncommon and when it occurs it is usually in lesions where the charred debris have not been properly removed. Cleansing with hydrogen peroxide is permitted where this seems to have occurred. In the rare cases where secondary infection warrants treatment, aureomycin ointment may be used

No scar formation is expected after treatment of superficial lesions such as common or seborrhoeic warts or telangiectases and the scars that follow deeper destruction are seldom unsightly Keloidal and hypertrophic scarring are exceptional.

Senile keratoses Small keratoses may be removed with the diathermy but the removal should be wide and deep If there is any suspicion of malignant change it is better to excise the lesion widely and check by histological examination.

Cutaneous horns if small, may be treated with diathermy Snip off horn and base for histological examination then destroy the underlying and surrounding tissue

Basal-cell epithelioma Small tumours on accessible sites such as the cheeks, forehead and neck are eminently suitable for diathermy removal A specimen for histological examination is first cut or curetted out. Begin diathermy by outlining the area to be removed and let the margin be well outside the apparent edge of the tumour since invisible undermining is common Increase the strength of spark and burn and scrape alternately until apparently well into normal tissue No dressing is usually applied

Lesions up to 0 5 cm diameter heal in 2 to 3 weeks leaving a negligible scar Larger lesions heal more slowly and leave obvious scars Lesions over 1 cm diameter are best treated by excision

Granuloma pyogenicum is best treated by diathermy Set the machine to produce a strong spark and transfix the lesion near its base Switch on and wait until the lesion cooks. With larger lesions several transfixions may be required Be ready to work quickly as brisk bleeding may occur as the needle is removed Remove the desiccated lesion and be ready for renewed bleeding as the base is destroyed to a depth where only normal oozing occurs.

Hairy non-pigmented moles may be removed with the diathermy provided they are small (under 0 25 cm) or in a position where a little scar will be unimportant. Larger moles are better excised. Destruction should go on until all the noticeably hard mole tissue has been scraped out

Skin tags are picked up with forceps and the stalks cut through with diathermy Seedlings without stalks are sparked so that they swell Anaesthesia is usually unnecessary

Telangiectases and spider angiomas are treated by transfixion with the finest needle and momentary sparking Blanching shows that the purpose is accomplished In some spider angiomas destruction of the central spot is enough but in others

the limbs will be seen to require treatment as well. Repeated treatment will be required for multiple telangiectases of the nose or cheeks as the blanching eventually occludes the view. This procedure is impossible under local anaesthesia.

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CHAPTER V

ALLERGY AND HYPERSENSITIVITY

ALLERGY

The word allergy is used to define the state that may be induced in certain individuals in which they will react against a specific substance that in the normal individual, causes no abnormal symptoms This reaction may be one of hyper sensitivity or of hyposensitivity but in general the term allergy refers to hypersensitivity

The allergic reaction is apparently an antigen-antibody reaction, but it is not always possible to demonstrate the presence of antibody An allergic reaction never occurs immediately after the first contact with the allergen but only after what we may call an incubation period of seldom less than ten days and sometimes much longer even months or years This hiatus between first contact and first symptoms helps to distinguish an allergic reaction from one due to a primary irritant. The latter causes a reaction on any tissue a few minutes to a few hours after first contact

A primary irritant may also be an allergen e g any skin will react against strong sulphuric acid but a skin that has become allergic to it will react against weak solutions which no longer irritate the normal non-sensitive skin In an allergic reaction there is little relationship between the quantity of allergen and the degree of reaction it causes e g in a person sensitive to a sulphonamide the reaction to 0 1 g will probably be just as severe as that to ten or twenty times the quantity

The presence of antibody can in some cases be demonstrated by the use of passive transfer tests. In the Prausnitz Küstner test, blood serum from the sensitized individual is used and in the Urbach Königstein test blister serum from an existing lesion or from one raised artificially with croton oil This serum is injected intradermally into a normal control a

day later the same area is injected with a solution of the allergen and if antibody were present in the serum of the suspect a wheal appears after 6 to 24 hours. The experiment is controlled by injecting two sites with suspect serum and two with normal serum one of each is later injected with the allergen, the other two with saline. It is probable that antibodies are carried by the lymphocytes.

The physiology of the allergic reaction is still unclear The precise nature of the end product of the antigen-antibody reaction is not known, and it is probable that the end product is not always the same but in some cases it may be histamine or a histamine like substance The end product stimulates effector organs in the skin, especially in the blood vessels, and the resulting vascular reaction is probably the basis of all the various pathological changes that may follow Even in allergic reactions produced by allergens acting on the skin surface the vascular reactions are of prime importance. It has been demonstrated that antigen-antibody compounds formed in the epidermis must reach the dermal vessels before the complete picture of oedema, spongiosis and vesicle formation can appear

In an allergic reaction the capillary blood vessels of the dermis or the arterioles and venules of the deeper layers may be affected. The type of skin reaction depends to a degree on the size of the affected vessels. The first major phenomenon in an allergic reaction is an exudative explosion in and around the walls of the vessels and at the same time there is a varying degree of cell necrosis. In this acute phase, according to the importance of one or other of these processes, one may classify cases into two clinical and histological types

1 Acute exudative allergic reaction (e g urticaria)

2 Acute necrotic allergic reaction (e.g papulo-necrotic tuberculide)

If at this point the allergen is removed the whole process is reversed and the skin returns to normal. If however the allergen remains active for a long time chronic allergic reactions may be seen

3 Chronic rheumatoid allergic reaction (e.g rheumatic nodules)

4. Chronic tuberculoid allergic reaction (e g tuberculosis, tuberculoid leprosy)

In these chronic types, which are commonly caused by microbic allergens there are necrotic changes in and around the blood vessels and a leukocytic infiltrate. Bacteria are seldom seen, however as they are destroyed in the reaction

Allergens A great variety of living and inert substances may act as allergens and may be classified thus

A Primary exogenous allergens.
  1 Inhaled dusts and vapours
  2 Contact allergens *dusts, liquids and solids.*
  3 Foodstuffs.
  4. Medicaments ingested injected or applied
  5 Microbes
  6 Parasites

B Secondary exogenous allergens
  1 Physical media such as heat cold pressure and exertion These probably act by causing some alteration of body proteins and the new formed substances may serve as allergens
  2 Certain foodstuffs and other ingested substances may become allergens after partial or complete digestion

C. Exogenous haptens.
  A hapten is a substance which alone is not an allergen but which when bound to serum or tissue proteins may acquire allergenic properties Examples are arsphenamine and phenolphthalein.

D Endogenous allergens
  1 Auto-endogenous allergens
  Tissues altered by inflammation trauma, cancer etc. may become allergens Some examples are urticaria in the prodromal stage of infective hepatitis urticaria or dermatitis with cancer urticaria after severe bruising of the skin or other organs The non specific rashes of the reticuloses are probably autoallergic reactions.
  2 Hetero-endogenous allergens
  Allergens may originate from parasites, microbes or fungi in the body

The clinical picture is not always of great help in the recognition of the cause or even the type of cause, of an allergic rash. An eczematous eruption (erythema, oedema, vesiculation, oozing, crusting and scaling) may be caused by a contact allergen or by one that is ingested, inhaled or injected. A generalized eczema suggests that the cause is being disseminated by blood spread localized lesions are usually due to a contact allergen. The eczematous reaction is a very common one, but there are many other types, e.g urticaria erythema multiforme erythema nodosum bullous, vesicular and pustular rashes and rashes that resemble those of diseases such as acne (bromides and iodides) lichen planus (gold, Mepacrine) and pityriasis rosea (bismuth)

It must be remembered that the type of reaction to an allergen is not always the same in different individuals or even in the same person in different attacks e.g a patient becomes allergic to sulphonamides and his first attack is one of urticaria while the second is an eczema. A person sensitive by contact to a substance will almost certainly react to it if it is given orally or by injection.

Some allergens may act on more than one organ. Such is the case with pollens that may cause dermatitis, hayfever and asthma. Alterations in the blood picture may accompany allergic eruptions eosinophilia is common and leukopenia and thrombocytopenia are less common findings.

The history is of the greatest importance in investigating any allergic disease One must know what the patient encounters in his work and what his hobbies are Has he changed his job or handled new substances before the disease began? Are the symptoms worse on working days than at weekends, and do they improve when he goes away on holiday? Are symptoms worse in the morning or in the evening? Have any new clothes, soap or cosmetics been used? What are his habits in regard to purgatives, tonics, sedatives, etc ?

The investigation of an allergic disease is an exercise in detection and no clue must be ignored A sensible patient who can correlate cause and effect will usually quickly find the cause (if it is not disclosed at once by the history) when the nature of the disease and the need for careful and constant observation are explained to him. He must be warned that the

incubation period for an allergic disease may be long and that the cause is not necessarily a thing that has recently come into his environment The nature of a thing long used may have changed (e g a new perfume in old standard cosmetic) or he himself may have changed

Serum sickness

Serum sickness is an allergic reaction that develops in humans between 8 and 12 days after a single injection of a foreign animal (e g horse) serum When large amounts of serum are injected the reaction is produced in about 50 per cent of cases In persons already sensitized the latent period is shortened to 5 to 7 days, but immediate severe and even fatal anaphylactoid reactions may occur The serum is believed to stimulate antibody formation which usually takes 8 to 12 days, and they combine with the remains of the allergen to precipitate the primary reaction The presence of antibody in the blood of patients suffering or having suffered, from serum sickness is demonstrable by passive transfer tests. Precipitins that combine *in vitro* with horse serum may also be present in the blood

The first sign of disease is often regional adenopathy and this is followed by fever joint pains, pruritus and an urticarial rash Morbilliform scarlatiniform and haemorrhagic eruptions are less often seen angioneurotic oedema may occur

Patients dying of serum sickness may show vascular lesions like those of periarteritis nodosa and this latter disease has been reproduced in experimental animals sensitized to foreign serum

The steroid hormones are very effective in treatment.

Anaphylaxis

Anaphylaxis is an allergic phenomenon demonstrable in experimental animals the guinea pig is most susceptible Very small quantities of the allergens usually proteins given subcutaneously will sensitize the animal larger quantities must be given if the intravenous route is chosen When the allergen is reinjected after a latent period there follows within a few minutes to half an hour a state of anaphylactic shock char

acterized in the guinea pig by itching dyspnoea and choking and, shortly death from suffocation

It is uncertain whether true anaphylaxis occurs in man, but similar anaphylactoid reactions are sometimes seen. The features are collapse, dyspnoea and asthma, convulsions and urticaria, proceeding sometimes to coma and death

The reacting tissues are apparently the capillaries, which become more permeable and permit extravasation of fluid and the smooth muscles which go into contraction, hence the dyspnoea and asthma. Passive transfer tests reveal the presence of circulating antibodies, and precipitins may also be present. Anaphylactic shock may be due to release of histamine or histamine-like substances as the syndrome can be imitated by injection of histamine

Anaphylactoid reactions may be seen in man when serum is administered to sensitized individuals. Reactions may also occur in sufferers from atopic sensitization when an atopen to which they are sensitive is administered intravenously or even intracutaneously as in testing or in desensitization Reactions to drugs, especially when these are injected, may reproduce the picture of anaphylactic shock, but the mechanism involved is different from that in true anaphylaxis.

Treatment is with the steroid hormones and in the hyper acute case an intravenous injection of a soluble cortisone preparation should be given. If this is not available adrenalin should be given intravenously

The Sanarelli-Schwartzman phenomenon

This is a non-allergic hypersensitivity reaction that may be licited experimentally in rabbits The animal is prepared by an intracutaneous injection of a bacteria-free filtrate or washing from a bacterial culture (e g typhoid bacilli) When the same or a different, filtrate is injected intravenously twenty-four hours later a haemorrhagic and necrotic reaction develops at the site originally injected this precipitating injection must be intra enous. This local reaction is known as the Schwartzman phenomenon.

When the filtrate is injected intravenously at twenty-four hour intervals generalized necrotic vascular reaction with

multiple haemorrhages and fatal termination takes place This is known as the Sanarelli phenomenon

The second or precipitating injection need not even be a bacterial filtrate agar or starch solution or foreign serum will serve as well Not all bacteria contain the principle staphylococci and streptococci are unsuitable Neisseria and *B coli* are very active

Laboratory animals apart from the rabbit react little or not at all The reaction is inhibited by heparin perhaps by stopping thrombus formation Heparin is formed and stored in mast cells as the rabbit has no mast cells this may explain its susceptibility

These reactions can only be produced if the interval between preparatory and precipitating injections is between 12 and 32 hours Allergy is obviously not involved because no antibodies are produced and there need be no relationship between the preparatory and precipitating factors and the state of reactivity is of limited duration

It is uncertain whether these phenomena occur in man but a picture comparable to that of the generalized Sanarelli reaction is seen in the Waterhouse Friderichsen syndrome with meningococcaemia and in patients dying suddenly after repeated intravenous injections of typhoid vaccine used to produce artificial pyrexia A great number of conditions such as *pyoderma gangrenosum nodular dermal allergides* and necrotic reactions following injections of vaccines have been cited as possible examples of the Schwartzman phenomenon and Gougerot even proposed a group of Sanarellides no proof of the theory is forthcoming

THE ARTHUS PHENOMENON

The Arthus phenomenon is a violent local allergic reaction demonstrable in experimental animals (usually rabbits) and occurring rarely in man The reaction develops after repeated intradermal or subcutaneous injections of foreign serum Injections are given every few days not necessarily into the same site after a few injections oedema develops and after later injections necrosis occurs This phenomenon was sometimes seen in man in the days when repeated injections of

large doses of antitoxins (horse serum) were commonly given.

The Arthus phenomenon may be reproduced in passive transfer experiments. The antibody is a precipitin which causes flocculation *in vitro* when mixed with the antigen. *In vivo* the antigen-antibody mixture causes, by some unexplained mechanism, constriction of arterioles leading to necrosis of the tissue supplied by them.

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in the lower layers of the epidermis and a monocytic infiltrate from the dermis.

Apart from the vesicles and inter and possibly intra cellular oedema in the stratum Malpighii, there develop also hyperkeratosis and patchy parakeratosis. Lymphocytes predominate in the vesicles of allergic eczema, polymorphs in that due to primary irritants. In some cases there is a loss of the epidermis in parts so that the tips of dermal papillae are exposed (eczema pits, *puits de Devergie*) In the healing stage there is at first acanthosis and parakeratosis before normal keratinization is re-established. The dermis is oedematous and shows a perivascular lympho-histiocytic (monocytic) infiltrate. The histological picture does not give any indication as to whether the basic lesion of allergic eczema is dermal or epidermal.

Civatte's suggestion that the primary changes in allergic eczema is an epidermal cellular degeneration followed by immigration of round cells and terminating in the *vésiculette primordiale* would, at first sight, imply that the mechanism involved in contact eczema was entirely different from that in other allergic skin diseases where the major changes begin in the blood vessels of the dermis. It has been experimentally shown, however that the whole picture of eczema cannot develop if sensitized skin exposed to the allergen has no contact with the vascular system of the dermis. Further eczema can result not only from contact but also from ingested allergens (e.g sulphonamides act in both ways) In eczema the primary combination of allergen with antibody (carried by lymphocytes) may well take place in the epidermis, but the intervention of vascular changes, characteristic of other allergic diseases, is of major importance in completing the reaction.

Haxthausen's experiments with homografts in identical twins has shown that contact dermatitis can only be produced when a certain factor (antibody) reaches the epidermis from the blood of a sensitized person. Normal skin reacts to the allergen when transplanted on a sensitized host, but skin from a sensitized person transplanted on a normal host does not react when the allergen is applied.

Micro-organisms as well as inert substances may produce the picture of eczema and the phenomenon is seen in ringworm

CHAPTER VI

ECZEMA AND DERMATITIS

THE word eczema means literally to boil over or break out There is no specific disease, eczema and the term has been and still is, used in different senses by different writers It is now used for describing skin lesions where on a basis of erythema, papules, vesicles oedema and scaling arise All or only some of these features may be present so that one may see an erythemato-squamous eczema, an erythemato-papulo-vesicular eczema, etc. The lesions may be dry or moist (weeping eczema) and excoriation crusting lichenification and pigmentary changes may arise as secondary phenomena in fresh or old lesions Dermatitis, inflammation of the skin is synonymous with eczema There is no hard and fast rule about the use of the terms dermatitis and eczema but it is my custom to employ eczema for those conditions where the cause is uncertain (e g nummular eczema) and dermatitis where it is (e.g allergic contact dermatitis due to a specific substance)

Eczema or dermatitis is an extremely common phenomenon and is often but not always due to an allergic reaction. The picture may be produced also by primary irritants and by bacterial or fungous agents (which may of course also act as allergens) and by causes as yet unidentified.

Histopathology The histological changes at various stages in allergic contact eczema have been fully studied in experimentally produced lesions but the sequence of events is still disputed According to Civatte the primary change is the degeneration of a few subcorneal cells towards which monocytes and lymphocytes migrate from the dermis this results in the formation of a minute *vésiculette primordiale* Spongiosis, rupture of intercellular bridges and the formation of a subcorneal or high intra-epidermal vesicle follows *Altération cavitaire* and reticular degeneration of the epidermis may also be seen Miescher however insists that the first changes are of spongiosis



Fig. 6

Allergic contact dermatitis.

Top: Hatband. *Middle:* Eyeshadow. *Bottom:* Nail varnish.

fungous infections not only at the site of infection but sometimes also at a distance (ide reactions) The role of bacteria in the causation or perpetuation of eczema and dermatitis has been well studied The bacterial flora of eczematous lesions is much more profuse than that of normal skin and it is likely that the micro-organisms can and sometimes do act as allergens. This property is quite unrelated to their pyogenic powers. Cutaneous sensitivity to bacteria (*Staphylococcus aureus* in particular) is markedly increased in eczematous as compared with normal subjects as demonstrated by tests with living organisms or broth filtrates This is a line of research which may yet prove fruitful but has so far given few practical results antibiotics have only a limited value in the treatment of eczema.

In many cases of eczema it is probable that more than one causative factor is involved and that the patients may be sensitive to a variety of contact and ingested allergens.

The factors inherent in the individual that predispose him to eczema are another subject for speculation Abnormalities in the liver bowel kidney and sympathetic nervous function have all been postulated as having a role and there are cases where it seems incontestable that this is so Endocrine factors are certainly involved at times as demonstrated by fluctuations of the eczematous state in some women according to pregnancy or even to the menstrual cycle Certain cases of eczema bid fair for inclusion in the group of psychosomatic diseases, but this is too often suggested as a means of avoiding the trouble of finding a physical cause this is not to say however that emotional influences may not have a bearing on the fluctuations of eczema An inherited predisposition to eczema is known to exist and is most obvious in the case of atopic eczema

ALLERGIC CONTACT DERMATITIS

The type of reaction produced in the skin by a contact allergen is almost invariably eczematous At first there is erythema and this is followed by varying degrees and combinations of oedema (which may be very marked in eyelids or genitals) vesiculation (microscopic or macroscopic) oozing crusting and desquamation Itching is always present and

Forehead. All the causes listed above and materials and dyes in hats and hatbands.

Ears As for the scalp nail varnish, spectacle frames, nickel or chromium plated earrings.

Eyelids and face As for the scalp cosmetics, including nail varnish, shaving soaps and lotions, air borne dusts and vapours (Fig 16)

Nose Nasal drops, sprays, etc dye in handkerchiefs.

Lips. Lipstick (whole lip affected) toothpaste plates of false teeth (worst at mouth corners) and mouthwashes fruit juices and occasionally other foodstuffs.

Neck As for the scalp dyes in clothing furs, scarves and ties. Nickel or chromium plated necklace clasps.

Hands, forearms and face Soaps, detergents, hand lotions and cosmetics dye in gloves, watch-straps, etc. resins and plastics plants, trees pollens and woods. Common offenders in the last group are primula, chrysanthemum, tulip narcissus, tomato, fennel, mayweed, poison ivy khak weed acacia cedar teak, imbuia and



Allergic contact dermatitis due to dye in clothing

in the acute phase the picture may be obscured by erosions and secondary infection as a result In the subacute phase dusky erythema and scaling predominate and in chronic cases the skin may become lichenified pigmented and cracked

Lesions almost always appear at the point of greatest contact with the allergen and may remain localized or spread after a time because the allergen is taken to other areas or because it is absorbed at one spot and disseminated by the bloodstream. In the case of floating dust or vapours lesions are usually first seen on exposed parts, friction points and the



Fig. 17
Allergic contact dermatitis due to plastic watch-strap.

moist skin folds. The area or areas affected may therefore be a guide to the type of allergen to be suspected It is quite impossible to list all the known causes of contact dermatitis and the list grows longer every day The common contact allergens affecting various skin areas are shown below Contact allergic reactions to medicaments cosmetics and industrial allergens are considered separately

Scalp Scalp lotions and tonics (usually containing mercury salts or resorcin) hair dyes (usually paraphenylene diamine) detergent and medicated shampoos

Thighs and legs. Clothing articles carried in the trouser pockets (e.g. matchboxes) plants and dusts. Dermatitis from nylon stockings may affect the whole area covered or it may be localized, and is always worst, at the friction areas of the feet and on the moist skin behind the knees the cause is the dye and not the nylon itself. Nickel or chromium dermatitis from suspenders is common reactions at a distance, often flexural



FIG. 20
Allergic contact dermatitis due to nickel.
B. Barnet)

are often seen in chronic cases and may be mistaken for atopic eczema (Fig. 20)

Ankles and feet. Dyes, plastics, rubber or other constituents of shoes, socks or stockings, arch supports, dusts and plants.

CONTACT DERMATITIS MEDICAMENTOSA

Dermatitis from the local application of medicaments is extremely common today The worst offenders are penicillin and sulphonamide ointments and lotions, closely followed by antihistamine ointments, local anaesthetics and disinfectants Dettol, iodine flavines) (Fig. 21) Such preparations should

mahogany The hands may become sensitive to the sap of fruit and vegetables prepared in the kitchen Javel and floor or furniture polish (Fig 17)

Axillae Deodorants, dress shields and material or dye in clothing

Trunk Material or dye in clothing cosmetics soaps and disinfectants. Dermatitis from clothing (khaki is a common



Fig 19
Allergic contact dermatitis from chemical contraceptive

[J F Schneider]

offender) affects the moist areas and friction points it may be frankly eczematous, but often it is a dry scaling diffuse brownish rash with fine punctate purpuric haemorrhages. Generalized rashes also follow absorption of an allergen from a localized primary source (Fig 18)

Perianal Ingested foodstuffs or drugs in process of excretion, soap enemas clothing and toilet paper (especially when coloured newspaper etc is used)

Genitalia Clothing (including jock-straps) and contraceptives (Fig 19)

eczematous or of a different nature entirely Local application of sulphonamides, for example, may cause eczema *in situ* and erythema multiforme elsewhere.

If a person becomes sensitive to a medicament (or other substance) he often simultaneously becomes sensitive to substances which are closely related chemically A patient allergic to sulphonamides may also react to novocaine and similar local anaesthetics, paraphenylene diamine hair dye and synthetic rubber This phenomenon is known as cross-sensitivity

CONTACT DERMATITIS FROM COSMETICS

Cosmetics and toilet preparations are among the commonest causes of allergic dermatitis in women and are relatively common causes of dermatitis in men.

Shampoos (especially detergents), hair fixatives (gums and resins) hair tonics and lotions (quinine, tar products, rubefacients, mercury salts and perfumes) and brilliantines cause the majority of cases of dermatitis beginning on the scalp or on the adjacent skin of the face neck and ears. A postauricular intertrigo is often due to such a cause Less common but much more violent are the reactions produced by hair dyes, particularly paraphenylene diamine (Fig 22) In such cases the area eventually affected may be very great (shoulders, arms, conjunctiva, even exfoliative dermatitis) Cold permanent waving is not particularly liable to cause trouble except on the hands of hairdressers, but allergic dermatitis may arise from the setting agents (resins) and primary irritation from the



FIG. 22
Allergic contact dermatitis due to paraphenylene diamine.
[Dr Gardner]

only be prescribed if it is felt that they are absolutely necessary in a given case and patients should be warned of the danger of sensitization so that they may stop treatment at once if it occurs It is safe to say that at least 10 per cent of patients using the *first three substances* mentioned *will become sensitized if they* use them for any length of time either at a stretch or intermittently The use of such things or any other known allergen



Fig 21
Allergic contact dermatitis due to penicillin ointment.

in the treatment of an allergic disease due to some other cause is pure folly as the chances of sensitization are even higher than usual If secondary infection in an allergic disease requires the use of antibiotics locally or systemically one should prescribe neomycin, aureomycin terramycin, or chloromycetin whose liability to sensitize is small. Streptomycin a major contact allergen, has fortunately not become popular for local application.

With medicaments the eruption usually begins (in previously insensitive patients) at the site of application and then spreads around this area or may become generally disseminated by absorption and cause lesions at a distance that may be

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FIG. 22

Allergic contact dermatitis due to paraphenylene diamine.

[G. [illegible]]

Shampoos (especially detergents) hair fixatives (gums and resins) hair tonics and lotions (quinine, tar products, rubefacients, mercury salts and perfumes) and brilliantines cause the majority of cases of dermatitis beginning on the scalp or on the adjacent skin of the face, neck and ears. A postauricular intertrigo is often due to such a cause. Less common but much more violent are the reactions produced by hair dyes, particularly paraphenylene diamine (Fig 22) In such cases the area eventually affected may be very great (shoulders, arms, conjunctiva, even exfoliative dermatitis) Cold permanent waving is not particularly liable to cause trouble except on the hands of hairdressers, but allergic dermatitis may arise from the setting agents (resins) and primary irritation from the

only be prescribed if it is felt that they are absolutely necessary in a given case and patients should be warned of the danger of sensitization so that they may stop treatment at once if it occurs. It is safe to say that at least 10 per cent of patients using the first three substances mentioned will become sensitized if they use them for any length of time either at a stretch or intermittently The use of such things or any other known allergen



Fig 2
Allergic contact dermatitis due to penicillin ointment

in the treatment of an allergic disease due to some other cause is pure folly as the chances of sensitization are even higher than usual If secondary infection in an allergic disease requires the use of antibiotics locally or systemically one should prescribe neomycin aureomycin terramycin, or chloromycetin whose liability to sensitize is small Streptomycin a major contact allergen has fortunately not become popular for local application

With medicaments the eruption usually begins (in previously insensitive patients) at the site of application and then spreads around this area or may become generally disseminated by absorption and cause lesions at a distance that may be

eczematous or of a different nature entirely Local application of sulphonamides, for example may cause eczema *in situ* and erythema multiforme elsewhere.

If a person becomes sensitive to a medicament (or other substance) he often simultaneously becomes sensitive to substances which are closely related chemically A patient allergic to sulphonamides may also react to novocaine and similar local anaesthetics, paraphenylene diamine hair dye and synthetic rubber This phenomenon is known as cross-sensitivity

CONTACT DERMATITIS FROM COSMETICS

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Axillary dermatitis is caused oftener by cream or stick deodorants than by liquids or powders. The allergen may be an excipient, perfume, benzoic acid, hexamethylene tetramine aluminium chloride or a disinfectant. The reaction may be eczematous or take the form of a pustular folliculitis (commoner with primary irritation, shaving) Sarcoid-like reactions due perhaps to zirconium compounds in stick deodorants have recently been described

Depilatories may cause severe primary irritation and allergic reactions on the face and legs The common depilatories of the past contained alkaline sulphides alkaline

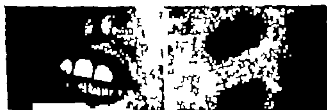


Fig. 24

Allergic contact dermatitis from lipstick. Positive patch test.

(Gawkrodger)

calcium thioglycolate, now commonly used seems to be a safer substance for the purpose.

Dermatitis may also be caused by hand-lotions sun-tan cosmetics, sun-protective applications and rubber powder puffs and in men by shaving soaps, creams, after-shave lotion, etc. Men sometimes become allergic to cosmetics used by their consorts.

Removal of the cause usually leads to rapid recovery except in the case of hair dyes where, for obvious reasons, the allergen cannot promptly be eliminated. Several brands of hypo-allergic cosmetics are on sale they contain bases, dyes and perfumes different from those normally employed. They are not quite so elegant as the standard cosmetics. They should be checked by patch testing before use, but a negative test does not mean that the patient may not become sensitive to them at a later date.

softeners (alkalis and thioglycolate) Rarely prolonged application makes the hair very brittle or even causes temporary alopecia from breaking of hair Frequent bleaching also dries the hair An unusual reaction from brilliantine made from poor mineral oil (old sump oil?) is oil acne of the forehead temples and ears (Fig 23)



Fig 23
Oil acne from brilliantine
[G. Garnier]

Creams and powders may cause eczematous reactions of varying degrees of severity that usually begin on and about the eyelids Creams are incriminated oftener than powders Rarely they cause pigmented dermatoses as a result of photosensitization by aromatic oils that they may contain Perfumes and toilet waters may also cause patchy or striped pigmentation for this reason (berloque dermatitis)

Lipsticks frequently cause dermatitis, usually of a chronic nature with scaling and cracking occasionally acute with oedema and vesiculation (Fig 24) This may be a primary allergic phenomenon or produced by photosensitizers used as colouring matters (eosin, dibromfluorescein or rhodamine B) If the dye is the sensitizer a stick coloured with carmine may be substituted.

Nail varnish is a frequent cause of dermatitis and primary lesions are unexpectedly almost never seen on the fingers. The skin of the face eyelids neck, ears, chest, axillae, arms, vulva and perineum are affected in that order of frequency and lesions are often unilateral as for example when a woman has the habit of resting her face on one hand The lesions are generally dry brownish and scaly but classical eczema may occur

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INVESTIGATION AND TREATMENT

Only one thing is likely to lead to rapid improvement and cure in contact dermatitis, as in any allergic disease and that is the identification and removal or avoidance of the cause If the cause remains the chances that the patient will cure himself by developing an immunity are small, and specific or non specific methods of desensitization usually carry little hope of success in contact allergic reactions

The duty is therefore, to make careful investigations and find the cause. We have already mentioned that the sites of the primary lesions and the history are of the greatest import ance In a difficult case however even with a sensible and co-operative patient, the search may be a long one.

When suspects are found they may be tested by removal and then by replacement if there is improvement or *patch tests* may be done. The rationale of patch testing is that although lesions may be present on only small or confined areas the whole skin is sensitive If the allergen is brought into relatively prolonged contact with normal skin the disease can be reproduced in a large proportion of cases

The technique is simple the allergen is applied to a piece of lint, cloth or gauze (four layers thick) the size of a postage stamp and put on the normal skin (hairless if possible) of the chest, back, inner side of the upper arm flexor surface of the forearm or the thigh When feasible apply the patches near the affected site Over the lint goes a piece of cellophane or other thin waterproof substance and the whole is sealed down with a generous piece of sticking plaster (e.g waterproof Elastoplast) The cellophane is used to protect the test area and the skin around it *in case the patient reacts to the plaster* The test takes forty-eight hours hence the necessity for using enough adhesive plaster to avoid accidental detachment In some countries the applicators can be obtained ready made and these save time when many tests have to be done It is essential to test each suspect under its own patch and not try to put several under one plaster Patients must be told that the patches are not to be removed save in special circumstances and that if the plaster becomes loose they must keep it in place with bandage or more plaster

If an allergen is also a primary irritant it must be diluted to a concentration which will not produce this latter effect. Tables of dilutions and diluents will be found in *Allergy* by Urbach or the *Year Book of Dermatology and Syphilology* 1957–1958 series. Dusts and powders are made into a paste with water before application. Patches are left in place for forty-eight hours before removal for reading results, but patients should be told that if it seems that a violent reaction is taking place before this time a corner of that plaster may be cautiously lifted for



Fig. 5

Allergic contact dermatitis due to streptomycin. Positive patch test and negative control.

inspection and the whole removed if it is so, replaced if it is a false alarm.

Positive reactions are eczematous and are graded thus

1 plus—erythema
2 plus—erythema and papules
3 plus—erythema and vesicles
4 plus—erythema and bullae

The test area in a positive reaction is elevated by oedema in most cases and this point may help in reading questionable results (Fig 25) Soap for example, often dries the skin and gives it a yellowish-brown shiny surface this is not an allergic reaction and there is no elevation. Sometimes there is no reaction when a patch is removed, but 24 to 48 hours later the

skin becomes red or brown and scaly in a delayed positive result. Patients should be told to note which patches itch because this symptom may be of decisive importance in interpreting dubious results. All the patches itch if the patient is sensitive to the plaster and when it is previously known that this is the case adhesive plastic tape, bandage or one of the modern hypo-allergic plasters should be used A blank control patch should be applied It must not be forgotten that the application of an allergen in a patch test may cause a flare up of the dermatitis

Positive results are of great value, but negative tests are sometimes seen even when it is certain that a person is sensitive to a given substance When a major suspect gives a negative result it must be ignored and a practical test made by removal for a time and replacement. Negative tests in such circumstances may mean that the degree of reactivity is not the same in all skin areas.

While investigation is proceeding treatment except in severe cases should be simple since the major anti inflammatory remedies may sometimes depress the reactions in patch tests Soap and detergents should not be used on affected areas oatmeal can be used instead Bathing in or wet dressings with potassium permanganate solution are usually well tolerated and calamine lotion or liniment are suitable applications

If the cause is eliminated cure usually follows quite soon in cases of short duration but may be protracted in chronic cases Sedatives for itch may be required and aspirin barbiturates or Serpasil (0 1 to 0 25 mg t.d.s) can be used The antihistaminics have no specific action in those cases where there is no urticarial element, but do often have a good sedative effect one of the best is Phenergan in doses of 0 01 g t d.s. or 0·025 g o n In the very severe case for immediate relief or to hasten resolution when the cause is removed ACTH and corticosteroid hormones give excellent results If the patient is in bed ACTH may be used in doses of 25 mg (aqueous solution) six hourly gradually reducing the dosage and eventually the number of injections with improvement. ACTH gel given once daily in the same way and with the same original total daily dose may be used for the ambulant patient but does not give quite such good results as the watery solution

in some cases. Corticosteroid hormones are normally used for ambulant patients and the dosage required at first is 100 to 150 mg. cortisone daily or the equivalent of this in one of the more recent derivatives dosage is tapered off with improvement. In mild and moderately severe cases where only a small area is involved, local applications of hydrocortisone lotion or ointment usually suffice.

Secondary infection is treated with aureomycin locally or systemically Chronic lesions are treated with Lassar's paste alone or with 5 per cent crude tar or with phenol and menthol ointment. X-ray therapy is occasionally necessary for chronic lichenified lesions.

Total avoidance of the cause or causes of allergic contact dermatitis is usually essential if the subject is to avoid recurrence This may mean hardship if the allergen is some essential substance for which no substitute can be found, but there is little point in wasting time on trials of specific or non-specific desensitization (by injecting foreign proteins, etc.) The chances of complete or speedy cure are not great in cases where the cause cannot be found or where the patient is unwilling to abandon its use (usually women and cosmetics)

ATOPIC ECZEMA

The term atopic eczema (or dermatitis) is used to describe a type of eczema which often occurs in fairly typical patterns in individuals with a family history of eczema, asthma, hayfever or migraine and may be accompanied by one or other of these diseases. The manifestations of atopic eczema are also described in the literature under such headings as infantile eczema, Besnier's prurigo, flexural eczema, constitutional eczema and generalized neurodermatitis to mention only the commoner ones. People with atopic eczema easily become sensitized to a great variety of common substances which they handle or ingest in everyday life and their sensitivity is demonstrable by positive reactions to scratch or intradermal injection tests with extracts of these and other substances. Unfortunately these tests do no more than indicate the susceptibility of the subject and the removal of substances giving a positive reaction is not

necessarily or even frequently followed by improvement. The presence of antibodies in the serum of such people is often revealed by passive transfer tests The term atopy (literally without place) was coined by Coca to differentiate certain forms of hypersensitivity in man from anaphylaxis in experimental animals and the concept has been broadened to that described above Atopic diseases do however arise in people



Fig 26

Atopic eczema in the infant.

presenting no family history of such disorders and may be induced in animals so that the term atopy should be taken as describing certain clinical signs rather than a particular immunological phenomenon

Atopic eczema is encountered at all ages but is commonest in infants, children and young people it presents slightly different pictures at different ages There is a clear tendency to spontaneous cure and symptoms seldom persist beyond adolescence but there are some cases which continue to relapse throughout life Asthma or hayfever may be associated

with attacks of eczema or alternate with them. It is impossible to predict which cases will clear spontaneously

ATOPIC ECZEMA OF INFANTS

This rarely begins before the second or third month and its appearance often coincides with the start of supplementary feeding The cheeks are first affected with an erythematous rash on which develop small papules and often vesicles. The lesions are moist, oozing, crusted and may become excoriated or lichenified from rubbing or scratching Spread of the original lesions may affect the whole face, scalp, ears and neck and other irregular patches appear especially on the forearms and wrists, legs and ankles (Figs. 26 27 and 28) The large skin folds are sometimes affected. Rarely the whole body is covered with an oozing erythroderma. The general health in the milder cases is often remarkably little affected, but the child is usually irritable and sleepless from itch Exacerbations frequently occur in relation to teething, colds or injections for immunization. Vaccination is absolutely contraindicated for fear of causing Kaposi's varicelliform eruption and the child should not be brought in contact with recently vaccinated people or those suffering from herpes febrilis.

Whether lesions are constantly present or relapse spasmodically most cases heal spontaneously without scarring, before the end of the second year in those who do not the pattern changes as they grow older

Treatment. The child should be protected against sudden temperature changes and not exposed to sun and wind. Wool clothing is always irritating cotton or linen are safest. Feather pillows and mattresses must be discarded and replaced by kapok or foam rubber The mother must be warned against indiscriminate trials of soap, detergents, antiseptics and medicaments prescribed by mothers-in-law kind friends and pharmacists

Bathing is usually well tolerated, but must be stopped if it is not. A pinch of potassium permanganate crystals may be added to the water making sure that all are dissolved before the child is immersed or a bag of oatmeal can be put in the water and squeezed like a sponge over the child. Soaking with olive oil or liquid paraffin may be necessary for the removal of

Fig. 27
Atopic eczema of infants.

Fig. 28
Atopic eczema of infants.

adherent scabs and scales. After a bath the skin is patted, not rubbed, dry and plain talcum powder may be used

The type of application used will vary according to the site to be treated and the reaction of the child but must always be simple and non-sensitising Calamine lotion or liniment, zinc cream (plain or with 5 per cent ichthyol) Lassar's paste (plain or with 5 per cent crude tar) may all be tried and discarded if not well tolerated Applications should be gently removed with a simple oil when necessary there are times, however especially with paste, when this should not be done too frequently a thick layer may be left over certain lesions to act as a protective cover Hydrocortisone ointments or lotions are often extremely effective palliatives but their cost precludes their use except in cases where lesions are acutely inflamed and relatively confined Antibiotic ointments (never penicillin or streptomycin, which are liable to induce sensitisation) are useful when secondary infection is present. Ointments containing antihistaminics, sulphonamides or local anaesthetics are barred because of their sensitising properties.

Antihistaminics by mouth are often useful for their sedative effect and may be given in the form of syrups or elixirs (e g Phenergan, Benadryl, Chlor-trimeton, etc.) in dosage appropriate to age. Attempts have been made to influence infantile eczema in a permanent fashion by long courses of corticosteroids or ACTH but although suppression of symptoms is often attained permanent cure has seldom been claimed and most cases relapse when the dosage is reduced below a certain level or when the treatment is stopped. These remedies, especially the corticosteroids, have a definite place in the control of severe attacks dosage should be very gradually reduced as improvement takes place.

The young infant should be prevented from scratching by the application of cardboard splints to the arms and the use of linen caps and masks if he rubs his head against the pillow These measures are rarely properly carried out as mothers imagine that splinting is cruelty to the child, but they are of major benefit when faithfully applied.

Food elimination tests must be done and any suspects rechecked and completely removed from the diet if they cause exacerbation of the disease. Common food allergens are cow's

milk pork fish (including cod liver oil) egg
citrus fruits cheese wheat and cereals and c
is implicated it may give trouble in any form
if boiled and skimmed five times or if recon



Fig 29
Atopic eczema in a hild

or other powder W unacceptab is to replac possible with soya bean suggested as but it is no obtainable and will not drink be used in pla In testing all of the diet mus and not o mentioned abo allergens identif should not be g until the child free of symptoms a year Any ne added to the diet tried one at a tim their effects may b

When home treatment fails the infant should be a to hospital where the environmental change often has effect even though the method of treatment is uncl relapse may occur on return home In very rare cases with eczema die suddenly often in hospital, and for no ap reason after a short spell of hyperthermia and collapse

ATOPIC ECZEMA OF CHILDREN

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are the flexures of the elbows and knees, the wrists and the neck, where excoriated papules are seen on plaques of brownish, lichenified skin (Figs 29 and 30) Around these plaques on the



FIG. 30
Atopic eczema in child.

limbs, and more rarely on the body or face, are more discrete, papular scratched lesions.

Attacks are followed by remissions lasting weeks or months and there is, as in infantile eczema, a definite tendency to spontaneous cure this usually occurs before puberty All manner of allergens may be involved, but it should be remembered that contact allergens assume more importance in the child nd the adult than they do in the infant. Most cases are worst in winter and this is due probably more to irritation

milk, pork, fish (including cod liver oil) eggs, tomato spinach citrus fruits cheese wheat and cereals and chocolate If milk is implicated it may give trouble in any form or be acceptable if boiled and skimmed five times or if reconstituted from one or other commercial powder When it is wholly unacceptable the best plan is to replace it as soon as possible with minced meat soya bean milk is often suggested as a substitute but it is not universally obtainable and many infants will not drink it Rice may be used in place of wheat In testing all the articles of the diet must be checked and not only those mentioned above Food allergens identified by test should not be given again until the child has been free of symptoms for at least a year Any new articles added to the diet should be tried one at a time so that their effects may be noted



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Atopic eczema in a child.

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lymphadenopathy of the type known as lipomelanic reticulosis may be associated Itching may be so severe that the patient scratches himself bare of epithelium in places or rubs his hair off, but secondary infection of an important degree is remarkably rare Cataract is a rare complication of atopic eczema in the older child or adult. Spontaneous cure is exceptional and most cases continue to suffer sporadically or continuously throughout life

The history and clinical signs generally point clearly to the diagnosis of atopic eczema, but occasionally the diffuse type may suggest the possibility of an erythrodermic eruption of lymphoma.

Treatment. The patient with atopic eczema must be instructed to observe himself carefully with regard to fluctuations in the state of his skin in relation to his daily routine, and to eliminate and recheck anything suspected of influencing him adversely Wool clothing, feather pillows, etc., should not be used and experiments made to find out whether soap is detrimental in any quantity or whether it may be used judiciously Scratch testing with dietary allergens generally produces many positive results which are non-specific in character and of no major help practical testing is necessary to determine what foodstuffs, if any should be eliminated. The results of scratch tests with inhalants (dusts, pollens, etc.) may be of some practical value in those cases suffering also from hayfever specific desensitization with extracts of the allergens so found to be suspect often does good for the hayfever and occasionally for the eczema as well.

Simple lotions, liniments, creams, pastes and ointments are used for local treatment many patients find that Vaseline or Ung emulsificans B P give them as much relief as anything Tar preparations such as Ether Soluble Tar Paste, Lassar's paste with 5 per cent crude tar or 25 per cent crude tar in acetone are often effective antipruritics so too, is phenol and menthol ointment. Hydrocortisone ointments or lotions are often of the greatest value for localized lesions

Sedatives such as the barbiturates, Serpasil or the antihistamines are often helpful and another drug that may benefit some cases is belladonna (e.g as Bellergal or Bellafolin) Non-specific methods of desensitization such as autohaemotherapy

from wool clothing than to climatic change It is often stated that patients with atopic eczema benefit from living in a dry warm environment, but my experience in the Transvaal which enjoys an ideal climate makes me doubt whether this is so

Treatment is on the same lines as that prescribed for adults

ATOPIC ECZEMA OF ADULTS

This almost always follows on eczema in infancy or childhood and seldom begins in a previously healthy adolescent or



Fig 3

Atopic eczema in nurse

adult When atopic eczema first appears in adult life the sufferer is often a woman whose hands are affected when she exposes them to increased trauma in a profession such as nursing or when she must do the washing for her first child

The lesions are usually lichenified plaques with scattered papules and, more rarely vesicles upon them (Fig 31) Sites of election are the flexures of the knees and elbows and the face (especially round the eyes and on the eyelids) neck, genitals and inner sides of the thighs. Any part of the skin including the scalp may be involved and although a patchy distribution is commonest a diffuse lichenification of the skin with much scaling (exfoliative dermatitis) may occur With this last form

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adult. When atopic eczema first appears in adult life the sufferer is often a woman whose hands are affected when she exposes them to increased trauma in a profession such as nursing or when she must do the washing for her first child

The lesions are usually lichenified plaques with scattered papules and more rarely vesicles upon them (Fig 31) Sites of election are the flexures of the knees and elbows and the face (especially round the eyes and on the eyelids) neck, genitals and inner sides of the thighs. Any part of the skin, including the scalp may be involved and although a patchy distribution is commonest a diffuse lichenification of the skin with much scaling (exfoliative dermatitis) may occur With this last form

lymphadenopathy of the type known as lipomelanic reticulosis may be associated. Itching may be so severe that the patient scratches himself bare of epithelium in places or rubs his hair off, but secondary infection of an important degree is remarkably rare. Cataract is a rare complication of atopic eczema in the older child or adult. Spontaneous cure is exceptional and most cases continue to suffer sporadically or continuously throughout life

The history and clinical signs generally point clearly to the diagnosis of atopic eczema, but occasionally the diffuse type may suggest the possibility of an erythrodermic eruption of lymphoma.

Treatment. The patient with atopic eczema must be instructed to observe himself carefully with regard to fluctuations in the state of his skin in relation to his daily routine, and to eliminate and recheck anything suspected of influencing him adversely Wool clothing feather pillows, etc., should not be used and experiments made to find out whether soap is detrimental in any quantity or whether it may be used judiciously Scratch testing with dietary allergens generally produces many positive results which are non-specific in character and of no major help practical testing is necessary to determine what foodstuffs, if any should be eliminated. The results of scratch tests with inhalants (dusts, pollens, etc.) may be of some practical value in those cases suffering also from hayfever specific desensitization with extracts of the allergens so found to be suspect often does good for the hayfever and occasionally for the eczema as well.

Simple lotions, liniments, creams pastes and ointments are used for local treatment many patients find that Vaseline or Ung emulsificans B.P give them as much relief as anything Tar preparations such as Ether Soluble Tar Paste, Lassar's paste with 5 per cent crude tar or 25 per cent crude tar in acetone are often effective antipruritics so, too is phenol and menthol ointment. Hydrocortisone ointments or lotions are often of the greatest value for localized lesions.

Sedatives such as the barbiturates, Serpasil or the antihistaminics are often helpful and another drug that may benefit some cases is belladonna (e.g as Bellergal or Bellafolin) Non-specific methods of desensitization such as autohaemotherapy

have now largely been abandoned as worthless Antibiotics locally or systemically may be necessary for secondary infection penicillin streptomycin and sulphonamides are to be avoided. The emotional state no doubt may influence the course of atopic eczema at all ages (though probably not quite so much as some writers would have us believe) and planned relaxation gives benefit in some cases where conditions of tension and stress are related to exacerbations

Corticosteroids and ACTH given over short periods are of the greatest value in controlling acute exacerbations. There are some cases of atopic eczema which resist all simple methods of control and cause the patient great misery and distress the corticosteroids may give relief at maintenance doses small enough to be safe and inexpensive

ECZEMA IN THE INFANT

Atopic eczema is not the only variety of eczema seen in infancy but it presents the greatest problems in the determination of the causes and in treatment Other varieties of eczema are equally common and of greatest importance are the infective eczemas which may be difficult to distinguish from atopic eczema especially when this is complicated by secondary infection Contact dermatitis is relatively rare in the normal infant except as a result of the use of medicaments and in such cases the history and the distribution of lesions usually make the diagnosis plain

INFECTIVE ECZEMA

Most cases of infective eczema in children are mild relatively localized and with appropriate treatment short lived only occasionally are they stubborn and chronic and even here the ultimate prognosis is always good, unlike that of atopic dermatitis which may be perpetuated into childhood or even adult life Infective infantile eczema is often described as seborrhoeic dermatitis or eczema but although the lesions of the two are similar in appearance and in cause it is not possible to postulate that seborrhoea exists in the infant and

there is no reason to believe that every infant with infective eczema will suffer from seborrhoea in adult life



FIG. 52
Infective eczema in infants.

The lesions of infective eczema often appear very early in infancy earlier than those of atopic eczema, but they may arise at any time The face or scalp is often first affected and the

lesions may be crusted or follicular and pustular like those of impetigo or they may be frankly eczematous patches (Figs. 32 and 33) In the latter case differentiation from atopic eczema is *quite impossible until the effects* of antibiotic treatment are seen The disease may remain confined to the face and head with moist, crusted lesions or dry reddish brown scaling plaques like *those which are known as* pityriasis streptogenes faciei in the older child There are often a few small follicular



Fig. 33
Infective eczema in an infant.

pustules especially at the hair margin and a postauricular intertrigo *with splitting in the furrow and an impetiginous* crust where the earlobe joins the cheek these points would suggest an infective rather than an atopic eczema The scalp may show scattered pustules or it may be covered by thick, adherent, oily yellow scales (cradle cap) Spread to the neck, body and limbs occurs less often than in atopic eczema, but when it does there is a predilection for the large folds of the axillae, groins and natal cleft where the skin becomes red the epithelium macerated and deep splits form



It is not common for the face to be spared when the body is affected

It is probable that this type of infantile eczema is the result of sensitization to, as well as infection by the causative organisms which are usually staphylococci or streptococci.

Treatment. In the majority of cases early treatment of the primary lesion with an antibiotic ointment (aureomycin, terramycin, neomycin, etc.) will result in speedy cure. Adherent scabs and crusts should, naturally first be removed by soaking with oil or starch poulticing In resistant cases which improve but relapse it is best to suspend treatment for a day or two before having the organisms cultured and tested for sensitivity to the antibiotics and begin again with the appropriate remedy Hydrocortisone-antibiotic ointments may be effective where antibiotics alone fail. Systemic antibiotics are rarely necessary Some difficult cases respond best to 5 per cent ammoniated mercury ointment or to 2 per cent sulphur and salicylic acid ointment the possibility of sensitization should be remembered when these are used. Complete resistance to such treatments raises the suspicion that the diagnosis is incorrect and that the case is probably one of atopic eczema.

ERYTHRODERMA

Erythroderma or exfoliative dermatitis in young infants is a relatively rare phenomenon. Congenital abnormalities of the ichthyosis group account for some cases while others are examples of infective dermatitis.

The infective erythrodermas are seen in infants a few weeks old and are usually described under the titles of Leiner Moussous syndrome or Ritter von Rittersheim's disease (Fig 34) There is no basic difference between the two conditions which are now recognized as, respectively relatively mild and severe generalized infective eczemas. The Leiner Moussous variety is a squamous erythroderma resulting from generalization of an infective eczema such as we have already described.

Ritter von Rittersheim's disease often begins with a fleeting bullous eruption (probably impetigo) around the mouth and this is followed by a generalized reddish purple erythroderma

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oftener and the liberal application of powder after cleansing Powder is suggested rather than some simple cream because the disease may be perpetuated by the over liberal application of unguents which may macerate the skin Silicone ointments (e.g. Coricone) do not have this disadvantage and are preferred by some to powder

Similar rashes may occur because the napkins are too rough, and allergic contact dermatitis may be caused by soaps and detergents used for washing the napkins or by the antiseptics in which they are rinsed



FIG. 35
Infective napkin rash.

Napkin rash is believed to be due in some cases to ammonia formed as a result of bacillary action on the excreta This can be eliminated by regular changing and prolonged boiling of soiled napkins or the use of disposable napkins.

In many cases, however there is an infective element and the lesions often spread to involve the skin folds and may rarely become generalized to produce an erythroderma. Sometimes erosions, fissures, vesicles or pustules may be seen.

A particular variety of infective napkin rash characterized by an erythema of the covered area with eroded papules on the convex surfaces of the thighs and buttocks, is sometimes

with peeling of the skin in large lamellae and sometimes flaccid bullae fever is the rule.

Treatment The prognosis of both the mild and the graver forms has been entirely changed by the use of antibiotics which should be given systemically except in the mildest cases. Penicillin by injection or one of the modern antibiotics by mouth are usually effective. Local treatment should at first



Fig 34
Infective erythroderma. Leiner Moussous syndrome.

be confined to bathing in potassium permanganate solution and the application of plain talcum powder In the healing phase residual patches can be treated in the same way as the ordinary localized infective eczemas

Napkin rash

A simple erythematous rash on the buttocks, thighs, lower abdomen and sometimes the backs of the legs and heels (but usually sparing the skin folds) may be the result of irritation from prolonged contact with wet soiled napkins. This is easily controlled by seeing that the napkins are changed

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described as post-erosive syphiloid of Sevestre and Jacquet. Congenital syphilis is excluded by dark-ground examination of serum from the lesions and blood serum tests for syphilis (on infant or mother)

Another variant of infective napkin rash is a chronic disease characterized by discrete large and small plaques of slightly-elevated dry scaly red to reddish brown skin (Fig 35)

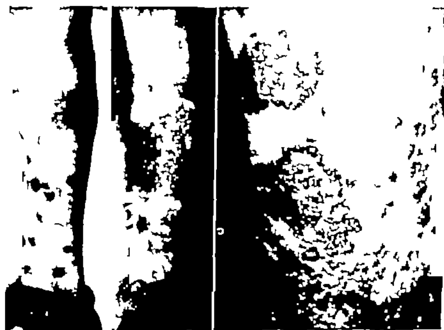


FIG. 36
Nummular eczema.

Treatment is with permanganate baths and the application of antibiotic ointments or hydrocortisone antibiotic ointments or lotions If ointments are not well tolerated drying lotions such as Castellani's paint or 2 per cent eosin in 5 per cent alcohol followed by dusting powder may be used

LICHEN STRIATUS

Lichen striatus is a relatively rare disease occurring usually in children and affecting the arms or less often the legs The lesions are unilateral in most cases and consist of small pink, yellowish or white lichenoid papules arranged usually in single file, in linear formation in the line of the limb

The streaks vary in length from a few centimeters to almost the whole length of the limb and may be continuous or broken. The appearance may be suggestive of a linear naevus or of lichen planus.

The histological picture is one of chronic eczema and the lesions disappear spontaneously in a few weeks to a month or two. No treatment need be given.

NUMMULAR ECZEMA

Nummular eczema is one of the commonest types of eczema of unknown origin encountered in adults. The lesions are usually small, discrete, oedematous, coin shaped patches of erythema studded with papules and vesicles and often moist and crusted scaling and lichenification may become marked in older lesions (Figs. 36 and 37) Peripheral spread and confluence sometimes produces large plaques. Sites of election are the dorsa of the feet, hands and fingers and the limbs. It is a stubborn disease which almost invariably runs a long relapsing course. Attacks are commonest in winter. Itch is often severe.



Fig 37

Nummular eczema.

It has been suggested that the dry asteatotic skin is most liable to be affected and it is true that the condition is aggravated by cold, dry conditions and by the use of soap and water. Whether nummular eczema is provoked by a variety of causes such as contact or ingested allergens, bacteria or primary irritants or is due to some single unidentified cause is a problem still unresolved.

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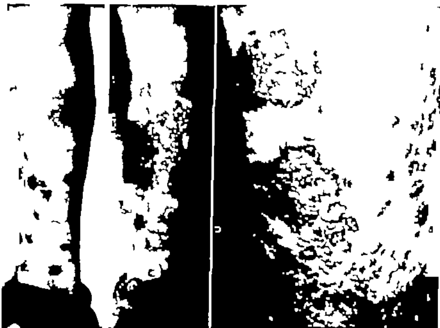


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Treatment Some cases are markedly influenced by the local application of antibiotic ointments (e.g aureomycin neomycin etc) or antibiotic hydrocortisone mixtures. Lassar s paste, plain or with 5 per cent crude tar is often effective and the patient should be told to keep the lesions continuously covered by addition of paste (and dusting powder to harden it if they wish) rather than constantly to irritate them by removal and reapplication Twenty five per cent coal tar in acetone and Ether Soluble Tar Paste may also be tried Sedatives such as aspirin antihistaminics Serpasil or barbiturates may be necessary for itch In severe and resistant cases systemic corticosteroid therapy may be necessary but the dosage usually required is low maintenance dosage may have to continue for a very long time

INFECTIOUS ECZEMATOID DERMATITIS

An eczematous eruption may arise in the immediate vicinity of or more rarely at a distance from, a discharging



Fig 38

Infectious eczematoid dermatitis with otitis media.

focus of bacterial infection such as chronic otitis media osteomyelitis or sinusitis (Fig 38) The cause is probably

sensitization to the bacteria which as already noted, may have allergenic as well as pyogenic properties Eczematous eruptions usually result from surface contact with the discharges, but blood spread may sometimes produce disseminated eczema.

Treatment. Treatment of the original cause is naturally most important, but there are times when it cannot be completely eradicated The organisms should be cultured and their sensitivity to antibiotics tested as a guide to proper choice of medication for use externally and, if necessary systemically as well. Antibiotic-hydrocortisone ointments are sometimes more effective than antibiotics alone in chronic cases As drying agents l'eau Dalibour and 2 per cent eosin in 5 per cent alcohol are recommended.

ECZEMA OF PARTICULAR AREAS

THE HANDS

Eczematous eruptions due to a variety of causes are extremely common on the hands of adults children s hands are rarely so affected perhaps because they are less susceptible to develop allergic contact dermatitis, certainly because they are less exposed to allergens than are adults. It was long believed that vesicular eczema of the hands, dignified by the term cheiropompholyx, was due to stoppage of sweat pores, but this theory has largely been abandoned. *Cheiropompholyx* is used today and less frequently with the passage of time, as a descriptive term for vesicular eruptions of the hands (*podopompholyx* when the feet are involved) where the cause is still unknown. The role of disturbances of the sweat mechanism in causing eczema is probably never more than secondary in that the sweaty macerated hand is more liable to be affected by primary irritants and contact allergens than is the normal.

The main primary irritants causing eczematous eruptions of the hands are alkalis (including soap and cement) acids and industrial solvents, and the skin so damaged is more than normally liable to become infected or sensitized. Natural defences against these irritants are the stratum corneum, the sebum and the sweat which is able, to a certain extent, to neutralize acids and alkalis.

Treatment Some cases are markedly influenced by the local application of antibiotic ointments (e g aureomycin, neomycin etc.) or antibiotic-hydrocortisone mixtures Lassar's paste, plain or with 5 per cent crude tar is often effective and the patient should be told to keep the lesions continuously covered by addition of paste (and dusting powder to harden it if they wish) rather than constantly to irritate them by removal and reapplication. Twenty five per cent coal tar in acetone and Ether Soluble Tar Paste may also be tried Sedatives such as aspirin, antihistaminics, Serpasil or barbiturates may be necessary for itch In severe and resistant cases systemic corticosteroid therapy may be necessary but the dosage usually required is low maintenance dosage may have to continue for a very long time.

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FIG. 38
Infectious eczematoid dermatitis with otitis media.

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Paget's disease It should be recalled that one of the sites of election for the lesions of scabies in women is the skin around the nipples.

THE LEGS

Infective eczema of the legs is fairly commonly seen in older people with a dry skin especially in the winter The skin particularly on the outer aspects of the leg has a cracked appearance (*eczéma craquelé*) with shingle-like scales curling up at the edges to reveal an underlying erythema (Fig 39) This may progress to a plaque or plaques of moist, vesicular or vesiculopustular eczema.

Treatment with antibiotic ointments is usually effective, but the patient should be advised afterwards to keep his skin lubricated with Vaseline or some similar simple emollient to avoid recurrence



FIG. 39
Infective eczema *Eczéma craquelé.*

HYPOSTATIC OR VARICOSE ECZEMA

This may be an isolated phenomenon or it may precede, accompany or follow on ulceration of the lower third of the leg. The lesion causing the primary skin manifestations is a thrombosing capillaritis, and an area showing punctate haemorrhages and pigmented spots (haemosiderin) may be noticed before ulceration takes place. The eczema which may follow ulceration is primarily infective but in chronic cases, where the patient tries every conceivable remedy contact dermatitis medicamentosa is often present as well and eczematous reactions anywhere on the body may also result from local absorption and blood spread of allergens (Fig 40)

Allergic dermatitis is due to a vast assortment of contact allergens encountered in and about the home and in industry As in eczema due to primary irritants the rash is often confined to and almost always worst on, the dorsa of the hands where the stratum corneum is thinnest.

Infective (bacterial) eczema usually begins on hands damaged by a primary irritant Nummular eczema is common on the dorsa of hands and fingers and some cases are infective in origin

Vesicular eruptions of the hands as a result of sensitization and blood spread of fungous elements or toxins from a primary dermatomycosis on the feet are so common that inspection of feet should be routine in any case of hand eczema where the cause is not at once obvious Similar eruptions are sometimes seen on the hands in cases of bacterial infections and allergic contact dermatitis of the feet. The only primary fungous infection of the hands likely to be confused with an eczema is that due to *Candida albicans*

Atopic eczema may affect the hands alone, but there is almost always the history and often other lesions to point to the way in which the case should be classified

Sensitivity to certain drugs may be manifested by eczematous reactions confined to the hands, but this is far less common than the erythema multiforme type of fixed drug eruption.

THE BREASTS

Eczema of the nipple area and surrounding skin may occur as a solitary phenomenon or as part of a more general affection. It is commonest in nursing mothers and during pregnancy The area involved may be small around the nipple, or extensive and both breasts are *usually involved a point of distinction* from Paget s disease The lesions are usually moist, cracked painful and slow to heal It is usually impossible to cure the disease while a child is at the breast and until lactation has been suppressed Once this has been done simple local treat ment with zinc cream or Lassar s paste is usually effective but hydrocortisone ointment can be used for stubborn cases When eczema of the breast *is very slow to heal*, and particularly when the disease is unilateral a biopsy should be done to exclude

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Hypostatic troubles are basically due to interference with the return of blood from the legs through the deep veins as a result of valvular deficiency (congenital or acquired) thrombosis etc Superficial varicose veins are not always a sign that a person is liable to develop an eczema.



Fig. 40

Hypostatic eczema and disseminated eruption du t treatment with sulphonamide ointment

The area affected may be relatively limited or spread to affect the whole leg and the dorsum of the foot The skin may be moist and sodden or it may be relatively dry red and scaly Frank ulceration may or may not be present In chronic cases the lower part of the leg is often oedematous and the skin and subcutaneous tissue may become quite woody and sclerotic. Lichenification and verrucous overgrowth of the skin as a result of lymph stasis (from recurrent cellulitis) occur sometimes.

Treatment. The best results are obtained if the patient is treated at first in bed, for several weeks if necessary until healing has obviously begun. It cannot be over-emphasized that generalization of eczema in such cases is almost invariably due to improper local medication, and potential sensitizers should only be used if the patient is under proper supervision he should be warned of the dire results of trying remedies of unknown content. Local applications of penicillin and sulphonamides cause endless complications in these cases.

For most lesions wet dressings with potassium permanganate or eusol, frequently changed, are often effective or the lesions can be painted with Castellani's paint. When the skin begins to dry it is best to leave it uncovered under a cradle. Antibiotic ointments (other than penicillin) also have their uses, but should be applied sparingly and stopped if the skin becomes sodden. In the healing phase bland applications such as calamine lotion or liniment or zinc cream may be tried, or phenol and menthol ointment if there is much itch Any application that seems to cause the slightest irritation should at once be discarded.

When the patient is ambulant supporting bandages will be necessary These may be of crepe if it is felt that occlusion is unwise and the bandage must be applied from toes to knee before the patient leaves his bed in the morning and removed only when he retires. Occlusive bandages are of great value, once eczema has been cleared or subdued, in the treatment of ulcers. Unna's paste, Viscopaste or Elastoplast all have their uses and should be removed and replaced every 5 to 15 days according to how they are tolerated Elastic stockings are worn after the eczema and ulceration are cured.

Surgical operations to re-establish the circulation carry no guarantee that they will influence the state of the skin, but plastic surgery is sometimes the only way of dealing with chronic ulceration

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Fig. 40

Hypostatic eczema and disseminated eruption due to treatment with sulphonamide ointment

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Fig 4
Erythema multiforme.

Fig 41
Erythema multiforme

[University of Cape Town (left)]

CHAPTER VII

ERYTHEMA MULTIFORME, URTICARIA AND ERYTHEMA NODOSUM

ERYTHEMA MULTIFORME

Erythema multiforme is an eruption that may be produced by a variety of causes usually drugs or micro-organisms it is probably always an allergic reaction. As the name implies the lesions are of various types and there are great differences in severity of the attack, but the background is always the same and there seems no reason to perpetuate the use of all the many names and subdivisions according to the clinical appearances and possible causes that have been used in the past.

The lesions are usually round and discrete 1 to 10 cm or more in diameter but if they are close enough together to overlap a polycyclic plaque may result. The common varieties are as follows red to bluish oedematous macules, papules or plaques annular lesions with a depressed healing centre target like patches of concentric rings of different colours, red bluish pinkish white bullae centrally situated on any of the above lesions. Haemorrhage into a bulla is not uncommon and colour changes as after a bruise may occur in the healing stage (Figs. 41 42 and 43) Sites of election in milder cases are the hands and feet (both surfaces) limbs and face in severe cases any part of the skin may be involved and the genitals and buccal mucosa very frequently suffer Bullous lesions are the rule in severe cases. An attack begins suddenly and lasts for one to several weeks, lesions appearing in crops. The lesions may itch but a burning pressing sensation of pain is commoner especially when tense skin is affected The life of an individual lesion is about a week.

When a drug is the cause the eruption may be relatively localized or generalized the attack mild or severe A great many drugs have been incriminated the first attack begins



FIG 4
Erythema multiforme

FIG 4
Erythema multiforme

[[illegible]]

only after a period of exposure usually not less than ten days and often much longer with drugs used only intermittently

A particular variety of erythema multiforme caused by drug sensitivity is known as *fixed eruption*. The name implies that the lesions persist or oftener always recur in exactly the same places Lesions of all types are seen but they are



Fig 43
Erythema multiforme
[University of Cape Town]

frequently bullous and it is commoner to see only a few lesions than a widespread fixed eruption When the cause is not discovered and recurrences *in situ* occur over months or years the affected areas become more and more pigmented until finally dark patches remain permanently between acute attacks (Fig 44) On a dark skin these patches often become pitch black. Frequently there is only a solitary lesion and in such cases sites of election are the palms lips, tongue or

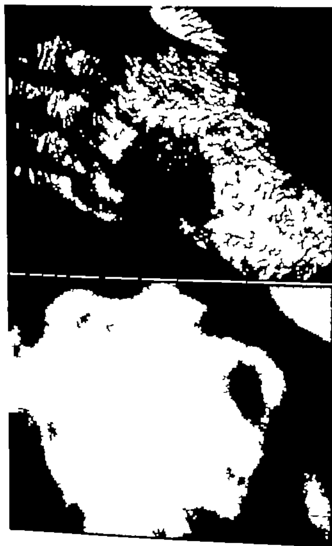


Fig. 44
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(Courtesy of Cape Town)

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soon become quite prostrated and even comatose. Bullae, usually haemorrhagic, appear in the mouth and on the lips and soon break to form painful, bleeding erosions or ulcers that hinder eating and drinking (Figs. 45 and 46). Similar lesions may appear on the nasal, conjunctival, genital and anal mucous



FIG. 45
Stevens-Johnson syndrome

membranes and surrounding skin. There is usually, but not always, a generalized eruption which may vary in intensity from a fleeting, blotchy erythema through all the varieties of erythema multiforme up to enormous bullae like those seen in pemphigus. Pneumonia occurs fairly frequently. The disease may be fatal and blindness may occur.

Another condition which is probably a variant of erythema multiforme is *toxic epidermal necrolysis*. This severe and sometimes

genital area. Mucosal lesions are, naturally eroded and many an unfortunate man with a genital erosion has been treated for syphilis when he was guilty only of taking the wrong purgative. Phenolphthalein is the commonest cause of fixed eruption closely followed by sulphonamides and salicylates, but many drugs have been implicated e.g aureomycin barbiturates arsenicals, streptomycin and potassium iodide A given person may occasionally react in this way to more than one drug e.g to both sulphonamides and salicylates.

Erythema multiforme may occur after severe sunburn, frostbite or deep x ray therapy presumably as a manifestation of sensitization to altered tissue and it has been reported as a symptom of infective diseases such as rheumatic fever tuberculosis vaccinia, septicaemia pneumonia diphtheria lymphogranuloma venereum and trichophytosis, to mention only a few It is possible that in some such cases medication was the cause and not the infecting organism but there is material in plenty to suggest that it is sometimes a microbic allergide.

In many cases of recurrent erythema multiforme there is a history that attacks are preceded by a cold sinusitis or tonsillitis, and that the rash appears whether the original disease is treated or not Erythema multiforme is exceptionally a manifestation of food allergy Recurrences *in situ* are occasionally seen in cases due to causes other than drugs

The vast majority of cases of erythema multiforme are not of major significance but a grave, bullous form occurs occasion ally and there is a tendency to classify it apart. The name *Stevens Johnson syndrome* has recently been attached to it in the Anglo-American literature, but it was first described forty years ago by *Fiessinger* and *Rendu* as *ectodermose érosive pluri-orificielle* Reawakening of interest in the condition followed the advent of the sulphonamides and I consider it to be simply a very severe type of bullous erythema multiforme It often follows the use of sulphonamides, sometimes other drugs but may appear for no obvious reason in which case it is probably a microbic allergide, a concept supported by the observation that the modern antibiotics are effective in treatment

The severe variety of erythema multiforme begins suddenly with high fever headache and malaise and the patient may

soon become quite prostrated and even comatose. Bullae, usually haemorrhagic, appear in the mouth and on the lips and soon break to form painful, bleeding erosions or ulcers that hinder eating and drinking (Figs. 45 and 46). Similar lesions may appear on the nasal, conjunctival, genital and anal mucous



Fig. 45
Stevens-Johnson syndrome

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Fig. 46
Stevens-Johnson syndrome.



Fig. 4
Toxic epidermal necrolysis.

(University of Cape Town)

fatal disease may follow the use of drugs and is characterized by flaccid bullae whose rupture denudes large areas to give the appearance seen in scalding (Fig 47)

Differential diagnosis In mild, non-bullous cases the lesions may suggest the related urticaria or erythema nodosum, which diseases may be considered as standing one on either side of erythema multiforme in degree of reaction. The common bullous type may resemble dermatitis herpetiformis, and the severe type acute malignant pemphigus or pemphigus vulgaris. Histological examination may be necessary in some cases to establish the diagnosis.

Histopathology There is oedema of both the epidermis and dermis with a perivascular lymphocytic and polymorphonuclear leukocytic infiltrate. Bullous lesions are formed by a cleavage at the dermo-epidermal junction the detached epidermis shows areas of necrosis, but there is no acantholysis. Multilocular bullae may be seen and sometimes a bulla may seem to be intra-epidermal as a result of irregular cleavage or regeneration of epithelium in its floor

Extravasation of erythrocytes, degeneration of endothelial cells of capillaries, and perivascular leukocytic infiltrates containing degenerate and fragmented nuclear elements are seen in haemorrhagic lesions.

Necrosis of the epidermis is extensive and diffuse in toxic epidermal necrolysis.

Treatment The cause must be found and eliminated if possible, and in mild cases this, with simple local applications, is usually all that is necessary Antihistaminics have rarely any major effect except as sedatives. When it is obvious that attacks follow tonsillitis or some similar focal infection appropriate action should be taken.

ACTH and corticosteroids have always a good and sometimes a spectacular effect on bullous erythema multiforme and should be used at once in severe and serious cases. ACTH in aqueous solution every six hours gives the quickest results ACTH gel or cortisone may be substituted, once recovery is assured for the tailing-off period. In the Stevens-Johnson type where the cause is apparently an infective agent and not a drug aureomycin should be given systemically not alone, but with ACTH or cortisone Dark pigmentation of the

affected skin remains after ACTH treatment in cases where melanocyte stimulating hormone is present as a contaminant this usually fades after some months.

Nothing need nor can be done about the pigmentation of fixed drug eruptions which will usually fade in time.

URTICARIA

Urticaria (nettle-rash hives) is so common that the average layman can recognize it. The characteristic, suddenly appearing lesions (wheals) which vary in size from papules a few millimeters in diameter to large regular or irregularly shaped plaques are pink or yellowish white, firm raised and itchy The eruption is usually generalized and covered skin is mostly affected lesions are often worst at friction or pressure points Typical true urticaria is rare in children under ten years and in the aged most cases of papular urticaria in children are due to insect bites. Bullous urticaria is usually a misnomer for erythema multiforme or insect bites Dermographism or factitious urticaria the appearance of wheals on rubbing or scratching the normal skin often occurs with urticaria but this phenomenon is seen in other diseases as well as in some completely healthy people (Figs. 48 and 49)

Giant urticaria (angioneurotic oedema Quincke's oedema) is considered as a separate disease by some writers. The lesions here are localized often to the face (eyelids, lips) or genitals, and consist of gross oedematous swellings. The mucous membranes of the mouth tongue, pharynx or larynx may also swell and cause embarrassment of deglutition and respiration and even sudden death.

The individual lesions of all varieties of urticaria are evanescent and disappear in a few hours to a day or two as suddenly as they appeared The course of an attack may be from a few days to a few weeks when the cause is active for only a short time but chronic persistent or relapsing forms, due to causes unknown lasting for many years are far from rare.

Urticaria is usually an allergic reaction and may be produced by a great variety of causes *It may be caused by the secretions* of plants and animals such as nettles, rues, geraniums,



FIG. 48
Urticaria.



FIG. 49
Dermographism. Factitious urticaria.

[Courtesy of Capt. [illegible]]

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triple response of capillary dilatation, escape of fluid into the tissues and reflex dilatation of arterioles)

Histopathology There is oedema of the upper dermis and a mild to moderate perivascular lymphocytic infiltrate in established lesions.

Treatment Of first importance is the discovery of the cause and its removal. This is usually simple enough in the case of urticaria due to drugs, but is not always so easy when food or other allergens are involved. Sometimes the patient will have to suffer a few attacks and take careful note of his actions before the attacks to determine the cause. And there are a great many cases, acute and chronic, where the cause can never be established. Scratch and intradermal skin tests may help in some cases, but the interpretation of results is not always an easy matter for the amateur or for that matter for the professional allergist.

Local treatment is of the simplest with cool baths, calamine lotion, loose clothing, etc.

The antihistaminics are of the greatest value in the average mild or moderate case. Phenergan (10 mg.) tablets or Benadryl (50 mg) capsules can be given, one every 2 to 4 hours these are the most potent, but have often a soporific effect not appreciated by ambulant patients. Where they are not well tolerated Anthisan, Diatrin or any of the other antihistaminics should be tried instead. In some cases a single dose of 25 mg Phenergan or one of the many prolonged-action tablets at night is all that is required in the healing phase. Antihistamine syrups for children and solutions for injection (for rapid action in severe cases) are also available.

It should, theoretically be possible to quell any urticaria by adequate doses of antihistaminics, but sometimes adequate dosage is in the range producing intolerable toxic effects. In cases of chronic urticaria or where the allergen is one known to be slowly excreted (e.g injected prolonged-action penicillin) treatment must be prolonged at suppressive levels for 3 to 4 weeks after the disappearance of symptoms. Penicillinase is reported to be rapidly effective against urticaria due to penicillin.

Calcium gluconate, 10 c.c. intravenously daily still has many advocates, but it rarely gives relief for more than a brief

caterpillars spiders, insects, etc. the lesions are usually localized to the area of contact, but in certain subjects generalized eruptions occur after repeated contact and may be accompanied by symptoms of severe shock. It is otherwise rare as a manifestation of contact allergy

Physical agents such as heat, cold effort or pressure and friction provoke urticaria in some cases. Lesions can be reproduced in such people by the injection of acetylcholine which may act by stimulating the parasympathetic system to release histamine like substances. Exposure to sunlight may cause urticaria and the wave length of the offending rays (which may be in the visible or ultraviolet range) can be determined.

Inhaled allergens (dusts moulds, pollens etc.) are rare causes of urticaria in normal or atopic subjects.

Foodstuffs are among the commonest causes and particular offenders are shellfish fish, eggs, pork, strawberries cheese, onions, garlic and chocolate. Some people are only affected if the food is not quite fresh others get attacks only at times of emotional upset

Medicaments, ingested or injected often cause urticaria they are discussed elsewhere.

Parasitic infestations such as hydatid cysts, intestinal worms (especially round worm in children) amoebiasis and malaria may cause urticaria and it may be a manifestation of sensitization to fungi and bacteria.

Autosensitization to products of cellular breakdown causes urticaria after severe bruising or in carcinoma of some organ. Urticaria was a prodromal sign of infective hepatitis in 10 per cent of a large series of cases I investigated during a war time epidemic.

As we have said, urticaria is almost invariably an allergic response due to an allergen-antibody mechanism even in the case of such agents as insect stings the variation in individual response (going as far as anaphylactoid shock) suggests that sensitization plays a part in some, if not all, cases. The presence of serum antibodies is demonstrable by passive transfer test in many cases of urticaria. The allergen-antibody product responsible for the reaction seems to be a histamine-like substance (histaminoid or H substance) and an urticarial reaction follows the injection of histamine into the skin (Lewis's

DDT powder between the child's sheets (every night) on carpets, furniture, floors, etc., and the application to the exposed skin of repellants such as citronella oil or Mylol when mosquitoes are also suspect. Pet dogs and cats must be regularly treated with flea powder and their sleeping places strewn with DDT. It is not always politic to be too plain-spoken



Fig. 50
Papular urticaria.
Left: Scabies. *Right:* secondary impetigo.

to some parents who are liable to flounce out at the suggestion of their having fleas in the house. In such cases prescribe 5 per cent DDT in calamine lotion to be applied at night.

The lesions themselves may be treated with calamine lotion, o with aureomycin ointment if there is secondary impetigo.

ERYTHEMA ANNULARE CENTRIFUGUM

This title is used for a variety of allergic reactions of the erythema multiforme and urticaria groups which are characterized by annular r circinate spreading lesions.

period. Calomel at night and a saline purge in the morning is a good old remedy in food allergy

For a very severe attack with symptoms of shock or for giant urticaria adrenalin 0·2 to 0 4 c.c hypodermically can be given in emergency and repeated every 2 or 3 hours while treatment with *ACTH* (by injection or intravenous infusion) or steroids is taking effect hydrocortisone preparations for rapid intravenous injection are now available for use in such cases. These last two remedies should not be used as a routine, but they are of the greatest value in severe cases and may be used in cases resistant to antihistaminics to shorten the attack after the cause has been removed dosage should be tailed off slowly

Other remedies sometimes effective in chronic cases are ephedrine aminophyllin histaminase and nicotinic acid.

Desensitization by exposure to small and then progressively increasing quantities of the causative stimulus is sometimes effective in cases due to physical agencies such as cold heat sunlight etc and it can be tried in food allergy

Treatment is naturally directed at the primary cause when urticaria is an ide reaction to some parasitic or bacterial infection or infestation

PAPULAR URTICARIA

Papular urticaria (strophulus, lichen urticatus heat spots, etc) is a common disease of infants and children occurring particularly in the summer months. It usually disappears before adolescence, but may persist into adult life. The lesions are red itchy papules or papulo-vesicles surrounded by a pink halo and are usually scratched and sometimes frankly impetiginized (Fig 50) They appear in crops, fresh lesions being seen in the morning for a week or two disappear for a spell and then recur It was long believed that this was a manifestation of food allergy and the significance of the fact that the disease promptly disappears in hospital but recurs on return home was not realized until quite recently

The vast majority of these cases are due to hyper sensitivity to insect (fleas, bugs, and occasionally mosquitoes) bites and prophylaxis consists in the use of Gamatox or

life of about three weeks, but new ones keep appearing for weeks or months. Such a picture has been seen in cases of internal cancer and with a variety of focal infections some cases may be manifestations of superficial trichophytons.

ERYTHEMA NODOSUM

Erythema nodosum is a fairly common disease affecting children and young adults, women oftener than men. The



Fig 52
Erythema nodosum

lesions are tender red to purple, nodular swellings or small plaques covered with shiny epithelium they appear nearly alway on both shins, but the thighs, arms and rarely other areas may be affected (Fig 52) There may be from a few to several dozen lesions that appear in crops over a few weeks to a few months. The life of a lesion is about three weeks, and as it heals the skin shows colour changes as in a bruise (dermatitis contusiformis) Suppuration does not occur

The acute forms are related to urticaria and may sometimes occur with frankly urticarial lesions. Attacks are short lived though recurrences are the rule in some cases. The lesions are small or large annular circinate or eventually polycyclic, flat or slightly elevated pink or red bands a few millimeters to a centimeter broad They may be seen in streptococcal infections such as rheumatic fever or tonsillitis or after the use of drugs such as salicylates

The chronic forms are related more to erythema multiforme but evolve slowly and progressively new lesions succeeding old



Fig. 5
Erythema annulare centrifugum (Darier)

ones or forming centrally as an old lesion spreads so that concentric figures are produced We are not concerned here with the annular lesions seen in specific diseases such as syphilis (recurrent roseola, annular erythematous gummas) tuberculoid leprosy reticulo-endothelioses or sarcoidosis.

In *erythema annulare centrifugum* (*Darier*) the rings, of which there may be several or many have a raised red rubbery edge and spread out to a diameter of 10 cm. or more before fragmenting to produce arcs of circles or polycyclic figures concentric rings are often seen (Fig 51) Each element has a

present in most cases these are radially arranged or pallisade structures composed of groups of histiocytes which occur in no other disease.

Treatment. The cause must be determined and removed or appropriately treated. In the streptococcal variety salicylates and antibiotics should be used. Antihistaminics have usually little effect, but ACTH and corticosteroids are effective in difficult (non-tuberculous) cases. Local treatment is unnecessary

Erythema nodosum occurs as a symptom of a great many conditions and there is some argument as to its nature most writers consider it as an allergide, but some believe it to be an entity caused by a specific infective agent which may be activated in a variety of circumstances as is the virus of herpes simplex

The most important cause of erythema nodosum is tuberculosis almost always a primary complex which can be demonstrated radiologically In such cases the tubercle bacillus is not demonstrable in the lesions but serial tuberculin tests may show increasing positivity Although tuberculosis is not the commonest cause of the condition it must be excluded in any case in a young person. Tuberculous erythema nodosum does not often recur

Streptococcal infections are commoner causes than the tubercle bacillus and recurrent attacks may follow attacks of *tonsillitis. Other diseases in which erythema nodosum has been* noted are scarlet fever rheumatic fever varieties of septicaemia herpes simplex, lymphogranuloma venereum (as the buboes soften) trichophytosis (kerion or after injection of trichophytin) coccidioidomycosis and many more. I have several times seen erythema nodosum appear during pregnancy because no obvious cause was found it is possible than an auto-allergic reaction was involved Drugs also may cause the disease, especially sulphonamides, salicylates, iodides and bromides. The so-called erythema nodosum leprosum is not a variety of erythema nodosum

The short life of a lesion and the absence of ulceration distinguishes erythema nodosum from syphilitic gumma and erythema induratum (but transition forms occur here) The distribution *is different from that of erythema multiforme* which is, of course, probably related

Histopathology The main changes are in the septa between the fat lobules of the upper hypoderm which are enlarged by a fibrinous and often haemorrhagic exudate containing clumps of polymorphonuclear leukocytes eosinophils and a few giant cells. Abscess formation and necrosis do not occur Vascular changes are usually extensive and severe especially in the larger arteries and veins (endothelial proliferation infiltration of walls) Miescher described reticulo-endothelial bodies

present in most cases these are radially arranged or pallisade structures composed of groups of histiocytes which occur in no other disease.

Treatment The cause must be determined and removed or appropriately treated In the streptococcal variety salicylates and antibiotics should be used. Antihistaminics have usually little effect, but ACTH and corticosteroids are effective in difficult (non-tuberculous) cases Local treatment is unnecessary

CHAPTER VIII

DRUG ERUPTIONS

REACTIONS of sensitization to medicaments applied to the skin are almost invariably eczematous but when drugs are used systemically by ingestion, injection or absorption through skin or mucosa the variety of reactions is much greater Individual sensitivity is the most important factor as a cause of drug eruptions but overdosage is implicated in some instances Once sensitivity is established the degree of reaction usually bears little relation to the quantity of allergen administered.

The incubation period between the first use of a drug and the first signs of sensitivity is seldom shorter than about ten days and may be much longer even months or years especially with drugs used only intermittently A person once sensitized to a drug generally reacts to it on every subsequent occasion that it is administered to him, and he will often react equally to chemically related substances e.g sensitivity to a barbiturate or to a sulphonamide usually means sensitivity to the whole group Occasionally a person may react only in special circumstances e g aspirin taken for a headache causes no trouble, but a rash appears if it is taken for a feverish complaint.

If a person is sensitive to a drug given systemically he will almost certainly react when it is used as an application on the skin and *vice versa* it is usually the case that sensitization is more readily induced by local application than by ingestion

People suffering from eczema are more liable to drug eruptions than are the normal and this fact is of great importance when contemplating the use of well known allergens such as penicillin or sulphonamides

Drug eruptions are sometimes accompanied by other manifestations of sensitivity and associated signs and symptoms may include malaise, headache fever ocular or aural disturbances, disorders of the haemopoietic system (leukopenia

thrombocytopenia) joint pains peripheral neuritis hepatitis gastro-intestinal disorders, nephritis, etc.

When sensitivity is established the use of the causative substance is followed after a short interval, sometimes only minutes and rarely more than a day by the rash. Once the pattern is established it seldom changes although sometimes a patient may have an urticaria on one occasion and another type of rash on the next. Removal of the cause is usually quickly followed by disappearance of the rash in the case of allergic eruptions pigmented lesions are the exception.

As nearly every drug has been implicated as causing sensitivity at some time or another only those often concerned will be considered.

COMMON DRUG ERUPTIONS AND SOME OF THEIR CAUSES

1 *Urticaria.* animal serum, bromides and iodides, atropine and belladonna, salicylates, barbiturates, opium derivatives, phenolphthalein, sulphonamides, penicillin

2 *Erythematous rashes* (roseolar morbilliform, scarlatiniform) arsenic, atropine and belladonna, balsams, barbiturates, quinine, bismuth, gold, salicylates, sulphonamides, penicillin.

3. *Eczema.* arsphenamines, sulphonamides, penicillin local anaesthetics, quinine and synthetic antimalarial drugs, gold, mercury antihistaminics.

4. *Exfoliative dermatitis* arsphenamines, gold, sulphonamides.

5. *Erythema multiforme* salicylates, sulphonamides barbiturates, phenolphthalein, arsphenamines

6. *Erythema nodosum* salicylates, sulphonamides, bromides and iodides.

7 *Acneiform pustular and granulomatous rashes* bromides and iodides.

8 *Purpuric rashes* arsphenamines, gold sulphonamides, balsams, carbamides, salicylates, barbiturates.

9. *Lichen planus-like rashes.* gold, Mepacrine.

10 *Keratoses* arsenic

11 *Pigmentary changes* arsenic, silver salts, bismuth

12 *Fixed eruptions* (usually erythema multiforme type, but sometimes eczematous, recurring *in situ*) phenolphthalein,

salicylates sulphonamides arsphenamines, iodides aureomycin, streptomycin gold flavines

ERUPTIONS CAUSED BY DRUGS IN COMMON USE

ACTH urticaria eczema, purpura.

Antipyrin and pyramidon erythema multiforme and fixed eruption erythematous urticarial and vesiculo-bullous rashes.

Antitoxins urticarial or erythematous rashes erythema multiforme purpura

Arsenic arsphenamines cause allergic eczematous erythematous and generalized scaling erythrodermic rashes long-continued use of arsenic by mouth may produce, sometimes years after stopping treatment warty keratoses especially on the palms and soles or a diffuse brownish pigmentation of the trunk dappled with drop-like paler areas (Fig 53) Zoster may occur during any kind of arsenotherapy

Antihistaminics eczematous rashes and erythema multiforme Sensitization is rare after ingestion common after local application

Aspirin localized or generalized pruritus, urticaria, eczema, erythema multiforme fixed eruption purpura.

Aureomycin pruritus and fixed eruption

Banthine dry mouth eczema, exfoliative dermatitis

Barbiturates erythematous rashes, urticaria, erythema multiforme purpura, stomatitis fixed eruptions, pruritus.

Belladonna and atropine erythemas, erythema multiforme purpura stomatitis fixed eruptions, pruritus

Benzocaine and similar local anaesthetics erythematous, urticarial and eczematous rashes Application is more liable to sensitize than injection

Bismuth injected bismuth causes a blue line on the gum margin stomatitis and sometimes erythematous, lichenoid eczematous or pityriasis rosea like rashes Accidental intra arterial injection causes gangrene of the wedge of tissue served by the vessel

Bromides acneiform papular and pustular rashes of the face, chest and back particularly bullous and nodular granulomatous lesions ulcers and erythema nodosum

Butazolidine erythema and aplastic anaemia

Chloral erythemas and rashes recorded under bromides.

Chloromycetin. pruritus ani, aplastic anaemia.

Chloroquine pruritus eczematous and lichenoid eruptions.

Chlorpromazine. eczema (mainly from contact) aplastic anaemia, hepatitis.

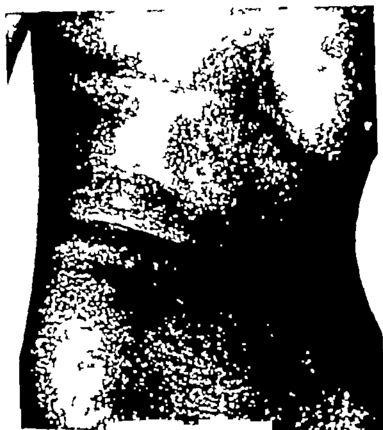


FIG. 53

Arsenical pigmentation.

Patient with epilepsy had been treated for three years with mixture containing bromide and liquor arsenicalis.

[*London Hospital*]

Corticosteroid hormones skin sensitization is very rarely seen. Eczema may follow ingestion or handling.

Digitalis erythematous and papulo-squamous rashes.

salicylates sulphonamides arsphenamines, iodides, aureomycin, streptomycin gold flavines

ERUPTIONS CAUSED BY DRUGS IN COMMON USE

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Butazolidine erythema and aplastic anaemia

Chloral erythemas and rashes recorded under bromides.

Phenacetin. erythema, urticaria, erythema multiforme and fixed eruptions.

Phenolphthalein. erythema, erythema multiforme and fixed eruptions which usually become darkly pigmented if not soon recognized commonest cause of fixed eruptions.



Fig. 55
Sulphonamide eruption
Note that exposed skin suffers most.

Potassium sulphocyanate. erythema urticaria, exfoliative dermatitis.

Quinine erythema, urticaria, eczema, purpura.

Salicylates erythema, urticaria, erythema multiforme and fixed eruptions, erythema nodosum

Silver salts local or general blue pigmentation, argyria, after long use.

Stilboestrol urticaria, eczema, exfoliative dermatitis, purpura.

Streptomycin eczema (at injection site or general) pruritus, erythema multiforme and fixed eruptions, exfoliative dermatitis. Local application is more dangerous than systemic use

Sulphonamides erythema, eczema, erythema multiforme and fixed eruptions, erythema nodosum, urticaria, exfoliative dermatitis, purpura. Eczema usually starts on exposed skin as sulphonamides are

Ephedrine erythema eczema, urticaria purpura.

Gold eczema (starts on exposed skin) exfoliative dermatitis, fixed eruption urticaria, lichen planus like eruptions of buccal mucosa and skin. Permanent pigmentation, chrysiasis, of exposed skin.



FIG. 54

Iodide eruption.

[St John Hospital]

Insulin. erythematous rashes, lipodystrophy and fat atrophy at injection sites.

Iodides acneiform rashes redness and swelling of face bullous, granulomatous and ulcerative lesions erythema nodosum Acne and dermatitis herpetiformis may be aggravated (Fig 54)

Mepacrine (atabrine quinacrine) erythema eczema urticaria, pruritus, stomatitis and lichen planus-like eruptions of skin and buccal mucosa. Blue discoloration under the nails

Mercury erythematous, multiform, urticarial and bullous rashes Gingivitis and stomatitis. Pink disease

Morphine (opium, codeine etc) pruritus erythema, urticaria

Para-aminosalicylic acid urticaria, erythema multiforme and fixed eruptions, lichen planus like rashes

Penicillin urticaria erythema eczema exfoliative dermatitis Lozenges may cause stomatitis or black tongue Urticaria may appear up to three weeks after an injection of long-action penicillin and tends to become chronic if not energetically treated

CHAPTER IX

INDUSTRIAL DISEASES

THE number of skin diseases which may result wholly or partially from the conditions of work is already vast and continues to increase as new processes and materials are used in industry The number of cases reported each year has been estimated as being today at least twenty times as many as a quarter of a century ago Industrial diseases can roughly be classified into those caused by primary irritants, allergic contact dermatitis, infections and cancers. The allergic conditions account for about 20 per cent of all cases. The causes may be solids, liquids or gases and of animal vegetable or mineral origin. It is no exaggeration to say that any chemical product may produce a dermatosis even water may be a cause. Many varieties of eruption are produced and lesions may be strictly localized or generalized

The tendency to dermatitis is, in some cases, governed by the type of skin and the susceptibility of the worker but there are some substances which affect a very high proportion of workers, e.g primula in florists and gardeners certain explosives such as TNT Sensitivity is not always limited to one substance cross-sensitization to related substances and plurisensitivity may well occur Dermatitis may begin soon after a worker enters an industry but in other cases it only appears after years of contact with the offending substance. The range of substances causing dermatoses naturally varies from one country to another and from one area to another but it is generally found that at the head of any list from an industrialized country one finds petroleum products oils and greases and alkalis, including cement and concrete causing between them 20 to 40 per cent of all reported cases. Other common causes are solvents, chromic acid and its salts, metals and metal plating dyes rubber and its compounds paints and varnishes, synthetic resins and plastics, terpenes and tar

photosensitizers (Fig 55) Use sulphonamides only when absolutely indicated as they are the most potent sensitizing agents in common use

Terramycin pruritus ani

Thiouracil stomatitis, erythema, exfoliative dermatitis. Agranulocytosis and hepatitis Depigmentation as a result of inhibition of melangogenesis

Vitamin B complex pruritus, erythema, urticaria, eczema.

Treatment Removal of the cause is all that is required in the milder cases which usually clear up fairly quickly The antihistaminics are useful for urticarial rashes and may have a sedative effect in others ACTH and corticosteroid hormones are used for severe cases dosage should be high for a day or two and gradually tailed off with improvement

Sodium chloride, 1 g four times daily hastens the excretion of bromides and iodides

BAL (British antilewisite dimercaprol) increases excretion of arsenic, gold and heavy metals give two ampoules, intra muscular thrice daily for two days then one twice daily for five days Penicillinase is rapidly effective in urticaria caused by penicillin

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gents better than the dry-skinned, but are more susceptible to trouble with oils, greases and dusts. The sweaty skin is most affected by alkalis.

Acneiform lesions are seen on the forearms, face and sometimes the thighs (impregnated overalls) in workers with compounds of chlorine and naphthalene, coal-tar products and coal dust, and most of all by mineral oils and greases. Secondary infection of the comedos is common and produces red, hard papules and pustules (Fig. 57)



FIG. 57
Oil acne.

Vesiculo-bullous eruptions, often secondarily infected, are produced by acids, alkalis, metallic salts, solvents, essential oils and some plants and bulbs. Erythemato-squamous rashes are caused sometimes by the same substances.

Dyschromias with hyper or hypo-pigmentation are seen in the chronic dermatoses of tar workers.

Tattooing is seen after explosions, but also occurs in miners, stone breakers and workers in electrolytic copper refineries.

Hyperkeratoses occur in workers with tar coal-dust and mineral oils and also in those who inhale or otherwise ingest arsenic (e.g. miners, dockers, farmers)

Ulceration and fissuring of the skin is usually the result of contact with strong caustics. One of the classical examples is the ulceration (circular punched-out ulcers) produced by chromium salts (chrome holes, *pigeonneaux*) on the fingers and

PRIMARY IRRITATION

The majority of industrial dermatoses are due to primary irritants which produce a greater variety of lesions than do contact allergens (Fig 56)

Eczematous reactions are common and often produced by alkalis acids and solvents The hands are usually affected and



FIG. 56
Dermatitis due to constant immersion in water in a fish-gutter

it is well to remember that among the important causes here are the substances used by workers for cleaning after work. Often enough a worker is unaffected by the prime materials he handles but abrades and degreases his hands by washing with paraffin (kerosene) or petrol and drying them on old sacking The modern detergents have the same effect in degreasing some skins Workers with oily skins tolerate alkalis and deter

on bulbs, harvest mites, moths and caterpillars, and *Ankylostoma duodenale*

ALLERGIC CONTACT DERMATITIS

As it is impossible to list all the industries and substances involved only a few important aspects of this problem will be given as examples. The industries where dermatitis is common are those concerned with building chemicals (organic and inorganic) dyes, explosives, pharmaceuticals, furniture, food stuffs, printing, hairdressing, rubber plastics and oil, but it is hard to think of any where dermatitis has never occurred.



FIG. 59
Cement dermatitis and positive reaction to 5 per cent potassium bichromate.

It has recently been shown that a major factor in cement dermatitis is that workers become allergic to chromium salts in the cement (Fig. 59) Sensitivity can be demonstrated by patch testing with 0 5 per cent solution of potassium bichromate in the majority of cases. The reaction produced is usually an erythema, sometimes with vesiculation, that spreads over the whole area covered by the plaster and often takes weeks to disappear Chromium salts are also causes of allergic dermatitis in the match industry in makers and users of some varieties of javel in workers repairing diesel locomotives (radiator fluid) in photographers and in workers in a variety of industries.

Carpenters and cabinet-makers often become sensitive to wood dust, which may cause asthma and hayfever as well as

nasal septum (Fig 58) A recent addition to this group is the granulomatous ulceration caused by implantation in the skin of particles of aniline and beryllium (histological picture resembling that of sarcoidosis)



Fig. 58
Chrome hole. Pigmentary
[London Hospital]

Mechanical irritation from friction may lead to corns and callosities with secondary burnitis and infection. Tiny fragments of glass metal plants, etc. may be rubbed into the skin and cause eczema or lay open the way to secondary infection or the penetration of other irritants Dusts can dry the skin and make it crack.

Excessive heat produces chronic reticular erythema (livedo reticularis) squamous erythema of exposed skin, intertrigo from sweating and prickly heat (miliaria rubra) in deep-level miners and stokers

Prolonged cold (refrigeration plants) causes or aggravates acrocyanosis and chilblains

Actinic rays cause dermatoses in seamen farmers, arc welders and cinema actors and aggravate existing lucites Photosensitizers such as tar products and dyes in the cosmetic industry increase the risk of actinic dermatitis.

Radiolucites are seen in workers with radium thorium, uranium x rays etc which are now more and more used in industry

In the group of primary irritants come also the infestations with animal scabies, *Pediculoides ventricosus* tyroglyphs acari

on bulbs, harvest mites, moths and caterpillars, and *Ankylostoma duodenale*

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dermatitis (Fig 60) Teak and satinwood are often implicated in Britain imbuia in South Africa Varnishes and solvents and preservatives in woods also cause trouble in these workers.

Hairdressers become sensitized by dyes rinses shampoos, permanent waving lotions etc. far oftener than do their clients.



FIG. 60
Imbuia wood dermatitis.

In the manufacture of drugs and antibiotics as well as in those who handle the finished products allergic dermatitis is common. Streptomycin is one of the greatest offenders and is a frequent cause of dermatitis of fingers and eyelids in nurses. Penicillin is less commonly implicated and other antibiotics only rarely Largactil (solution usually) is becoming well established as a common allergen and photosensitizer Local anaesthetics and plastics cause dermatitis in *dentists* *The* practice of putting a bowl of Dettol or some such antiseptic

solution by every wash-basin in some hospitals leads to sensitization of a significant proportion of nurses and doctors used in this way the disinfectant serves no useful purpose and is brought into unwarranted disrepute.

Many cases of allergic dermatitis in industry are caused by the antiseptics (iodine, flavine, picric acid) provided in first aid outfits. The substitution of a detergent (labelled with its full chemical constitution and not by name) has been suggested by the Workmen's Compensation Commissioner in South Africa and if this is followed it should reduce the risk very considerably

The lesions of allergic contact dermatitis in industry are usually eczematous (possibly complicated by infection) and begin at the point of greatest contact, usually the fingers, hands, and forearms. The allergen may be conveyed to the face and other parts by the fingers. In the case of dusts such as cement, lesions are also found at friction and sweating points such as the neck, axillae, elbows, waist, genitals and ankles.

The type of reaction may be a guide to the allergen in some cases. Agerite alba causes depigmentation as a primary phenomenon or after a mild eczematous reaction it is a substance used in the manufacture of certain rubbers and the hands are usually involved Rubber gloves used for protection in other industries may produce the effect as may elasticized material. The effect is striking on the black skin. Hyper pigmentation is seen in people working with photosensitizers.

INFECTIVE DISEASES

Coccal infections secondary to minor or major trauma are common in many industries. Pyoderma of the hands and arms and paronychia are common in the sugar and confectionery industries. Acute malignant pemphigus may occur in meat-handlers.

Anthrax is seen in farmers, those who work with hides and hair and i veterinary surgeons.

Erysipeloid is fairly frequent in butchers, cooks, tanners, fishermen and fishmongers and may occur in any worker handling meat, game or fish.

Tularemia may occur in people handling game (hares) and, more rarely is contracted indirectly from pricks or

abrasions by infected thorns etc. in the areas where the infected animals live.

Brucellosis attacks those handling sheep goats and cattle. Inoculation usually results in an ulcer with satellite adenopathy but sometimes erythemato-squamous and crusted lesions are seen In people frequently in contact with infected animals an allergic contact dermatitis of the forearms has been reported.

Glanders occurs in people handling horses but may also pass from man to man.

Verrucous tuberculosis of the hands is seen in handlers of meat, veterinary surgeons, doctors, nurses and post mortem room attendants

Doctors and nurses may contract syphilis accidentally and contamination during the performance of the treponemal immobilization test is reported Glass-blowers, shuttle weavers and musicians may be infected with syphilis about the mouth

Virus diseases transmissible to man from animals include cowpox horsepox milker's nodules orf aphthous fever epizootic pseudo-aphtous stomatitis and benign lymphoreticulosis (cat-scratch disease)

CANCER

Cancer as an industrial hazard is relatively rare but well recognized As will be seen it is often difficult to prove a relationship between cause and effect

Skin cancer usually basal-cell epithelioma may follow a solitary traumatic incident or it may appear in sites subject to repeated trauma

Burns may be followed by cancer but it is not always possible to decide whether the cause was thermal alone or perhaps also the burning agent (e.g tar)

Chemical trauma where a single exposure is postulated as the cause, is almost invariably accompanied by high temperature (petrol tar asphalt)

Long exposure to tar mineral oils soot, coaldust, etc. is well known to lead, usually after a stage of chronic hyperkeratotic dermatitis to cancer (Fig 61)

Cancer after radiodermatitis occurs in doctors, radiographers and radium handlers.

PREVENTION AND TREATMENT

Prevention of industrial dermatitis is more important than treatment for a worker once subject to disease, is often lost to the industry There is much talk of "hardening" where a worker eventually develops an immunity to the noxious substance. How often this occurs with minimal signs and symptoms is hard to say but once a person has shown signs of major intolerance it is rare, in my experience, that his skin ever completely recovers so long as he continues in the same occupation.



FIG. 6

Squamous-cell carcinoma and cutaneous horn in mule spinner

London H [illegible]

The worker with known irritants must be taught to avoid contact and must be provided with the necessary equipment to help him do so e.g. protective clothing and gloves, proper exhaust ventilation, fume cupboards, caps masks and goggles, forceps, etc. Barrier creams with a variety of bases and neutralizing agents are available as protection in certain industries if properly employed to protect the still healthy worker they are useful, but they are of little avail to the already sensitized person. The possibility of a barrier cream acting as a sensitizer must not be forgotten and it is probable that in most cases Vaseline is just as effective as complex remedies.

Workers must be taught to cleanse the skin properly and be provided with the most effective and inoffensive materials for the purpose The dangers of using industrial solvents for cleansing have already been mentioned

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the major suspects. A visit to the place of work or inspection of other affected workers may be indicated.

Patients with industrial dermatitis should be made to stop work or in minor cases, put to some inoffensive job while investigation and treatment proceeds. Treatment is essentially that described for allergic contact dermatitis with bland applications, sedatives and ACTH or cortisone if necessary Secondary infections are treated with antibiotics unlikely to produce further sensitization.

It is not unusual in the more chronic case to find that stopping work is not automatically followed by improvement. The reason may be in some cases that chronic infection has led to bacterial sensitization and this may be very slow in subsiding Sometimes it means that the cause was not encountered at work at all, but that it must be sought in the patient's home or leisure employment or pursuits. In some chronic cases radiotherapy may eventually have to be tried as a last resort, but it must be remembered that this does not permanently alter the patient's state of reactivity Outright settlement of a claim for compensation may be more effective than any medication

When it is found that a man should change his employment he must be advised what type of occupation he should seek and what he can and cannot safely handle.

Minor injuries to the skin must be properly treated at once and the use of allergenic applications strictly avoided workers should report signs of dermatitis immediately

After an initial attack of dermatitis there is no reason not to allow the worker to return to his employment for a practical test. In some cases there is no recurrence if he is more careful to avoid contact than in the past. In yet others there may be minor recurrences, decreasing in severity and hardening occurs but in a large percentage of cases the sensitivity increases with each trial of work and it becomes necessary to advise a change of occupation This is often a great blow for the skilled worker who cannot earn as much in any other capacity and many will struggle on in spite of great disability Sometimes it is possible for a sensitive worker to use an inoffensive substitute and in industries where dermatitis becomes common such changes are often forced upon the employer

In allergic contact dermatitis it has sometimes been possible to desensitize a patient by repeated patch applications of the allergen in very dilute solution at first, systematically increasing the strength if it is tolerated failures far outweigh successes

There is little to be gained by selection of personnel for hazardous industries except, naturally that persons with a history of allergic diseases should be rejected Prophetic patch testing with the allergens to be encountered is pointless because it is improbable that a person who has never been in contact with them will react and the act of testing may sometimes sensitize

In the investigation of a case of industrial dermatitis the history is important and a knowledge of the substances used by the worker essential Points of importance in diagnosis are that the condition appears during or within a short time after industrial exposure (there are exceptions in the case of tar radium etc) cessation of work is followed by improvement return to work results in exacerbation dermatitis begins in areas of greatest contact other workers are affected or the patient is known to be using a proved irritant or allergen In appropriate cases proof may be obtained by patch testing and it should be a rule to test all the substances used and not only

There is no constant relationship between the varieties of personality types and emotional disorders and the skin diseases so that no hard and fast rules for treatment can be suggested. It is true, however that removal of tension, anxiety or frustration may have dramatic effects in some cases, but it must be repeated that psychiatric treatment seldom takes priority over systematic investigation on standard lines.

CUTANEOUS NEUROSES

There are some skin diseases which are certainly the product of the disordered mind and require psychiatric treatment.

Acarophobia is a fear of parasitic infestation and the patient, who may or may not once have had lice or scabies, complains



Fig 62

Left Neurotic excoriations. *Right* Dermatitis artefacta. A wool-grader' attempt to simulate anthrax.

(D B Pfister)

of itch and produces epithelial scales that he has picked off in evidence of his complaint. *Syphilophobia* and *bromhidrosiphobia* are of the same order

Trichotillomania is a condition in which the patient, often an adolescent, produces alopecia by pulling out hair from the

CHAPTER X

PRURITUS, PRURIGO AND NEURODERMATITIS

PSYCHOLOGICAL ASPECTS OF SKIN DISEASES

It cannot be disputed that there often seems to be a relationship between the onset or exaggeration of certain dermatoses and functional nervous disorders but it is difficult to estimate the degree to which nervous instability is responsible for the appearance of skin lesions or to decide whether the nervous changes are the cause rather than the consequence of the skin disease The concept of psychosomatic dermatoses is not new although it has been popularized in the last twenty years especially by the Americans. Shock, strain and so on have long been mentioned in discussions of the causes of many skin diseases, but no attempt was made to define the relationship The main result of the study of psychosomatic disorders has been, frankly to provide a convenient method of escape from investigating the physical causes of many difficult cases by labelling them as due to tension, stress, or emotional instability This is unfortunate because these factors do often play a part in skin diseases but it is rare that the part is of such importance that a trained psychiatrist is likely to do more good than a common-sense practitioner or dermatologist.

The course of almost any skin disease may be influenced by emotional changes, but there are some conditions which regularly show this influence e g psoriasis seborrhoeic dermatitis and rosacea. Other conditions in which emotional disorders sometimes seem to have a major role are atopic eczema, chronic urticaria localized or generalized pruritus and eczema of the hands Sweating is of course so influenced Two conditions classified without major argument as frequently being genuine psychosomatic disorders are lichen simplex chronicus and alopecia areata

application of strong acids or caustics, injection of air under the skin, etc., but the picture produced seldom resembles in the

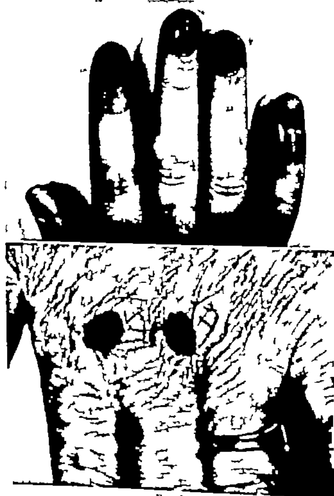


Fig. 64
Dermatitis artefacta.
Top From running needle under the nails. *Bottom* From application of caustic soda.

slightest any known skin disease in distribution or shape of lesions (Figs. 63 and 64) Proper occlusion of an affected area

scalp or occasionally eyebrows or other areas. In *trichokryptomania* the hair is broken off short by rubbing with the hand or a brush

Neurotic excoriations result from excavation of the accessible skin, frequently of the face with the nails or other instruments



FIG. 63
Dermatitis artefacta Lesion produced by *igniting cotton-wool soaked benzene*

(Fig 62) The patient usually has had some minor chronic complaint such as acne (*acné excoriée des jeunes filles*) or sycosis barbae, but this may long have subsided

Dermatitis artefacta Skin disease may be feigned by people seeking sympathy or to avoid working An enormous variety of lesions of the accessible skin (rarely an important part such as the hand) may be produced by sharp instruments, the

Temperature changes and extreme dryness cause some people to itch Pruritus may seem to be a pure neurosis in some cases.

In many cases it is not long before secondary lesions as a result of scratching appear in pruritus. These include erythema urticated lesions little excoriated, follicular "prurigo papules linear excoriations (make sure the patient is not suffering from lice or scabies) eczematous patches (primary or secondary?) pustules, boils, impetigo lichenifications, pigmentation and adenopathy

Regional pruritus

Certain skin areas are especially liable to chronic pruritus and lichenification due to causes which are sometimes identifi able, often not. It seems to me that in many cases where the cause is not found we are dealing with the results of a scratch habit in specially disposed subjects Whether this predisposition has an emotional or a physical basis (hypersensitive skin) is not clear Sufferers, almost invariably adults, are often notice ably tense and relaxation therapy may improve them. In any event it seems probable that such an individual starts scratching as a result of some transient infection or reaction of sensitiza tion, rubs the skin until it is lichenified and continues to scratch this abnormal skin even when the original cause has long disappeared. Sufferers will try any remedy and as a result often become sensitized to a great variety of locally applied medicaments.

Pruritus of the ano-genital region is the commonest example of this group but other areas which may be affected are the external auditory meatus (fungous and microbic infections seborrhoeic dermatitis, etc) nasal orifice (infection, ingrowing hairs) axillae mons veneris and ankles. Once pruritus-lichenification is established for six months or more it becomes excessively difficult to cure and cases giving a history of having been affected for ten or even twenty years are commonplace.

Pruritus of the scalp

This is a fairly common disorder It may be a pure pruritus, but excoriations, scabbed papules and even areas where the hair has been rubbed down to a stubble may be seen. In such cases look for signs of infestation, seborrhoeic dermatitis

is promptly followed by healing and the appearance of new lesions elsewhere if the patient is so inclined

PRURITUS, PRURIGO AND LICHENIFICATION

Pruritus simply means itch and the term is generally used in dermatology for conditions characterized by local or generalized itching in which there are either no skin changes or where such changes are secondary Prurigo is used in the definition of certain itchy papular skin eruptions and in a more general sense for itchy lichenified rashes (e g atopic eczema or Besnier's prurigo) Lichenification describes the thickened, leathery appearance of skin which has been subjected for long periods to scratching or friction

Itch or pruritus has long been considered to be a miniature pain, but the physical stimuli that produce pain do not, in smaller degree, invariably cause itch Recent experiments with cowhage, a vine with pods covered with tiny spicules that cause itch when they penetrate the skin have suggested that protein splitting enzymes acting on nerve endings or releasing some product from epidermal cells are at least sometimes the cause of itch *This process is unrelated to the histamine reaction* presumed to be involved in the itching of allergic diseases.

Generalized pruritus

Generalized itch may be a symptom of many systemic diseases and states such as diabetes leukaemia and diseases of the reticulo-endothelial system uraemia, liver disease (with or without icterus) cancer pregnancy and old age *It was my finding* during the epidemic of infective hepatitis in Britain between 1941 and 1944 that pruritus occurred much less frequently in patients with this disease or with homologous serum hepatitis than in those with obstructive jaundice Both the hepatic and the senile varieties of pruritus may be helped often considerably by testosterone given by injection or as sublingual tablets

Contact agents such as soaps, detergents bath oils and disinfectants may cause pruritus alone or as a preliminary to a dermatitis such is also the case with ingested or injected drugs.

can be used to wet a wick of cotton wool inserted to keep the skin surfaces apart. A sedative such as Soneryl 0 1 g or Phenergan 0·025 g should be given at bedtime as itching is generally worst in the night. It is surprising what improvement can be obtained with these simple suggestions. A hydrocortisone lotion may be used at the same time applied in minimum quantity twice or thrice daily

Often after initial improvement, the condition becomes static An application such as Dohi's paste may then be tried.

Shock treatment with 2 per cent sulphur and salicylic acid in 90 per cent alcohol is used for recalcitrant cases the percentage of successes is hard to judge as the reason why the patient does not return can only be guessed

Aureomycin or one of the other modern antibiotics will be used for infected lesions, alone or with hydrocortisone Penicillin, sulphonamides, local anaesthetics and antihistaminics must on no account be used locally Silver nitrate solution 2 to 5 per cent, is useful for cracks.

The prurigo group

Hebra s conception of prurigo as a distinct entity characterized by a disseminated eruption of little itchy papules has now fallen away and the term is used less and less as the causes of such eruptions become known It is still used, however for some conditions of known and unknown aetiology

Infantile prurigo is commonly called papular urticaria and is now known to be caused almost invariably by hypersensitivity to insect bites.

Prurigo of pregnancy begins about the fourth month and lasts until confinement. Pruritus, especially of the hands, feet and back, is followed by an eruption in these areas of small scratched papules. A therapeutic test may be necessary to distinguish this cond tion from abortive herpes gestationis. Treatment is purely symptomatic

Hutchinson s summer prurigo is one of the many manifestations of photosensitivity and is considered under the latter.

Winter prurigo or better pruritus, is a simple itch of the legs and thighs, sometimes the whole body occurring in winter and worst when the patient is undressing at night. Scratch

and chronic follicular coccal infections I have twice seen chronic lymphatic leukaemia begin in this way

PRURITUS OF THE ANO-GENITAL REGION

This is one of the most stubborn dermatoses The lesions are usually lichenified and there are spells of acute eczematization as a result of bad bouts of scratching or from sensitization to some local remedy The anal region (pruritus ani) the vulva (pruritus vulvae) or scrotum (pruritus scroti) may be affected alone but generally the whole ano-genital and perineal area is involved and lesions may spread right up the natal cleft and an inch or two out on to the buttocks or down the thighs. When the scrotum or labia majora are affected the lichenification may be very thick and almost woody

The causes (which may have disappeared before the case is seen) are various contact allergens such as soap paper (and printer's ink) clothing etc irritation as a result of lack of hygiene or from over scrupulous hygiene coccal and fungous infections (inspect feet for signs of dermatophytosis) ingested drugs such as purgatives and the modern antibiotics diabetes alone or with moniliasis chronic discharges from the vagina or rectum fissures and piles intestinal parasites (thread worms in children) enemas vaginal and rectal suppositories Psoriasis, especially in the elderly person attacked for the first time may present as a pruritus of this region In women over the menopause the possibility of leukoplakia and other precarcinomatous conditions must never be ignored and a biopsy specimen examined if there is the slightest suspicion

Treatment If a specific cause is found it must be appropriately treated In many cases the cause cannot be found at the first or any subsequent visit and symptomatic treatment is all that can be advised All treatments in use by the patient before examination are stopped and he is told to forbear from further self medication Moist cotton wool is to be used for gentle cleansing after defaecation and the area is not to be soaped in the bath Constipation should be treated with liquid paraffin taken in appropriate dosage after each meal The skin is often sodden and in such cases lotions such as calamine with 2 per cent phenol will be far better tolerated than ointments lotion is applied as required in the day and at night

Sometimes there is considerable psoriasiform scaling and in most areas the surface may be macerated.

Solitary lesions are the rule and there are never more than a few a point of importance in distinction from lichen planus which it may closely resemble. Biopsy is sometimes necessary to establish the diagnosis the histological picture is of a chronic eczematous reaction Papillomatous overgrowth of the skin is

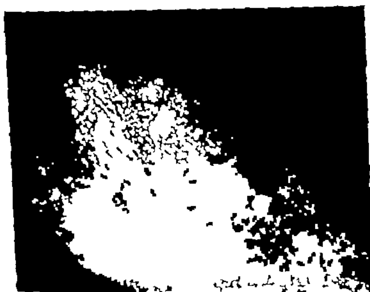


FIG. 63
Lichen simplex chronicus. Vulva...

sometimes seen in moist areas especially in the elderly The condition is extremely chronic and intractable and liable to relapse after any form of treatment.

Treatment It must be made plain to the patient that unless he is willing to help by conscious effort to avoid scratching, cure is unlikely Lassar's paste with 5 per cent tar 25 per cent ... in acetone and phenol and menthol ointment can first be tried, with sedatives if necessary Occlusion with Elastoplast for long periods is curative in some cases and x-ray therapy should be used in the most recalcitrant.

marks or a little lichenification may occur but no prurigo papules. Treatment is with simple ointment or antipruritics.

Hebra's prurigo It is very debatable whether such a condition exists as an entity The name is used to describe a chronic, very itchy small papular generalized eruption with secondary lichenification and excoriation This picture may be produced in childhood by papular urticaria and atopic eczema in adult life by atopic eczema infestations and non-specific eruptions of the lymphomas. Cases with severe itch have been described as prurigo ferox milder cases as prurigo mitis

Lichenification and neurodermatitis

It has already been mentioned that lichenification of the skin is the direct result of prolonged scratching and that it seems often to occur in predisposed subjects Here we are concerned with lichenification as an apparently primary phenomenon where no underlying cause can be determined Emotional factors are probably most important in some of these cases although it seems certain that some physical cause must precipitate the itch originally Primary lichenification is commonly seen in white people and Indians in South Africa but is exceptional in the more primitive Bantu.

Lichen simplex chronicus (névrodermite)

This is the commonest type of localized lichenification. The lesions are always situated on relatively accessible parts of the skin such as the nape of the neck (women particularly) thighs ankles (rubbing with the heels) or arms. (Fig 65) Some cases of ano-genital pruritus and lichenification could be classified in this category By the time the lesions are established it is generally impossible to discover what provoked the original itch.

The round or oval patch of skin involved varies in size from a few centimeters up to 10 to 20 cm. in diameter Pinkish at first, it becomes progressively deeper in colour and finally is brown or even black on a dark skin The central zone is of dark, thickened leathery smooth skin cross-hatched into lozenges by exaggeration of the normal tiny epidermal folds Around this is a band of lighter papulated skin and beyond this the lesion merges imperceptibly with the normal skin.

Sometimes there is considerable psoriasiform scaling and in moist areas the surface may be macerated.

Solitary lesions are the rule and there are never more than a few a point of importance in distinction from lichen planus which it may closely resemble. Biopsy is sometimes necessary to establish the diagnosis the histological picture is of a chronic eczematous reaction. Papillomatous overgrowth of the skin is

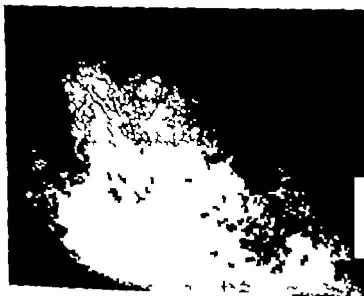


Fig. 65
Lichen simplex chronicus. [illegible]

sometimes seen in moist areas especially in the elderly The condition is extremely chronic and intractable and liable to relapse after any form of treatment.

Treatment It must be made plain to the patient that unless he is willing to help by conscious effort to avoid scratching, cure is unlikely Lassar's paste with 5 per cent tar 25 per cent tar in acetone and phenol and menthol ointment can first be tried, with sedatives if necessary Occlusion with Elastoplast for long periods is curative in some cases and x ray therapy should be used in the most recalcitrant.

DIFFUSE LICHENIFICATION

This is not a disease entity but may occur as a result of persistent scratching in a great variety of itching diseases such as eczema or dermatitis atopic eczema lichen planus and the reticulo-endothelioses. The vogue for labelling cases of diffuse lichenification as generalized neurodermatitis without looking for a physical cause is on the wane. Although tension and emotional disorders are often associated in such cases it must be realized that psychiatric treatment is of little value to a patient who is in fact suffering from some physical disease.

PRURIGO NODULARIS OF HYDE

Hyde's prurigo is a rare disease, perhaps a variant of lichen simplex chronicus which usually affects women between

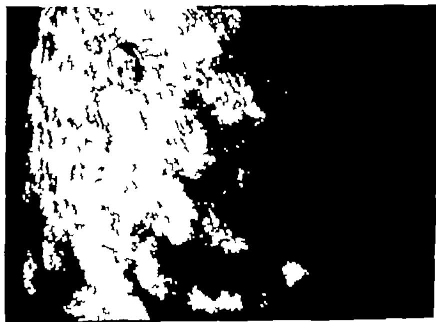


FIG 66
Prurigo nodularis of Hyde.

30 and 50 years The lesions are discrete, dome-shaped, firm, pink, itchy and often excoriated nodules 1 to 2 cm. in diameter The limbs are generally affected and there are seldom more than a few dozen lesions (Fig 66)

Histopathology There is acanthosis and hyperkeratosis and a round cell infiltrate in the dermis in which little nodules of hyperplastic nervous tissue can sometimes be demonstrated. An important degree of endovasculitis is also evident.

Treatment. No successful treatment for this extremely chronic disease has yet been found. Cortisone and ACTH have no effect and destruction with the cautery and radiotherapy are usually only of temporary benefit.

Exfoliative dermatitis and erythroderma

Under this heading are included all those conditions which produce a generalized erythema of most or all of the skin with oedema, scaling, lichenification and sometimes vesiculation pruritus, often intense, is the rule in adult patients. In some cases of unknown origin the names pityriasis rubra of Hebra and exfoliative dermatitis of the Wilson-Brocq type are used with the implication that they are diseases apart, but with advances in our knowledge these cases become rarer Acute and chronic varieties of exfoliative dermatitis occur but in no case is it wise to treat the condition lightly as a fatal outcome is possible no matter what the cause.

Exfoliative dermatitis may follow overtreatment of any relatively generalized skin condition, e.g it may be a complication of treatment of psoriasis with chrysarobin ointment and I have seen it occur when pityriasis rosea was mistaken for dermatophytosis and treated with Whitfield's ointment. Erythrodermic forms of psoriasis are well known and such a picture may also be produced in lichen planus, pityriasis rubra pilaris and atopic dermatitis.

Norwegian scabies and pemphigus foliaceus may both give a picture of exfoliative dermatitis. Many drugs but in particular the arsphenamines, gold and sulphonamides, may cause exfoliative dermatitis. Streptococcal infections in adults and in children (Leiner Moussous syndrome and Ritter von Rittersheim's disease) are also causes of erythroderma.

An important group is that in which erythroderma is a forerunner by long or short periods, of mycosis fungoides or a manifestation of one or other of the reticulo-endothelioses or haemopoietic diseases.

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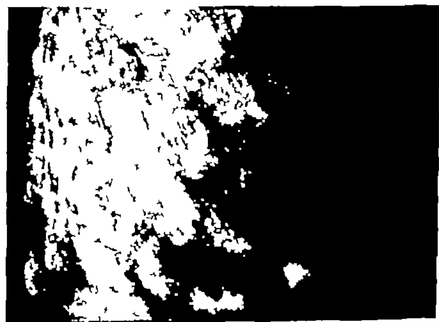


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vast majority of cases it is a benign and reversible change, but in a few cases it has been described in association with erythroderma due to some disease of the haemopoietic or reticulo-endothelial systems. The enlarged glands are firm and discrete and although easily visible are seldom enormously enlarged the condition is often mistaken for Hodgkin's disease (Fig 67)

Histopathology The major change in the glands is a reticulum cell hyperplasia in the medulla. Intracellular melanin pigment is scattered through the medulla especially in and around the reticulum cell infiltrates. Sinus or follicular hyperplasia is usually also visible.

In many cases biopsy of the skin and possibly a lymph gland and investigation of the state of the blood and marrow will be necessary to establish the diagnosis

The prognosis in many cases has been markedly changed for the better since the advent of the antibiotics, ACTH and corticosteroids

LIPOMELANIC RETICULOSIS

In some cases chronic exfoliative dermatitis is accompanied by a peculiar hyperplasia of the superficial lymph glands which



FIG 67
Lipomelanic reticulosis Cause undiscovered.

has been named lipomelanic reticulosis (Pautrier and Woringer) The condition is not linked to any particular type of dermatitis but may occur in erythrodermic psoriasis atopic eczema, Norwegian scabies arsenical or gold dermatitis, etc. In the

The capacity of the skin to rid itself of certain micro-organisms rests perhaps on more than one property and the relative importance of the various properties is still disputed. Chemical agents, such as fatty acids in the sweat and sebum the acid reaction of the sweat (acid mantle) and the electric properties of the skin, may all play a part and it is clear that desiccation leads to diminution of the bacterial flora while moisture increases it

The normal intact skin supports its resident flora without complaint and the microbes are very unlikely to become parasitic even after injury by cuts or wounds. The skin which has become more chronically altered by disease is prone to be invaded by pathogenic or potentially pathogenic organisms, and it is possible that even some resident saprophyte might become parasitic pathogenic organisms on the whole come however from external sources or from foci of infection elsewhere in the body

The establishment of infection on the skin is facilitated by improper treatment of injuries and dermatoses. Minor cuts and injuries are best cleansed with soap and water and no antiseptics should be applied their use is liable to facilitate infection by causing primary irritation and some are potent allergens. The risk of secondary infection in established dermatoses is increased by over treatment, by improper treatment with medicaments that cause allergic reactions and by occlusive dressings that keep the lesions moist.

When confronted with primary or secondary infective dermatoses use antibacterial agents which are unlikely themselves to induce sensitivity and if the response is not quickly satisfactory do not hesitate to have the organism identified by culture and its sensitivity to the various antibiotics determined before altering the treatment.

PYOGENIC INFECTIONS

IMPETIGO CONTAGIOSA

Impetigo is one of the commonest skin diseases of children and occurs either as a primary infection or as a secondary phenomenon in itching diseases such as scabies, head lice, etc.

CHAPTFR XI

BACTERIAL INFECTIONS

THE skin surface is never sterile and no reasonable amount of washing or application of antiseptics can make it so The micro-organisms found on the skin surface and in the orifices of the glands are in general saprophytes to which the skin is so accustomed that they seldom become parasitic and cause disease

The normal skin has a large resident flora of microbes which are virtually impossible entirely to remove and which will return in normal quantities after any process of cleansing or sterilization The common *resident saprophytes* of normal skin include both aerobic and anaerobic species aerobic organisms found are the Micrococci (Staphylococci) *M epidermidis* *M albus* *M candidus* and *M flavus* and the lipophilic fungi *Pityrosporum ovale* and *P orbiculare* and anaerobic organisms are *Propriomibacterium acnes* and *P saccharolyticus*

Almost any microbe, whether non pathogenic or potentially pathogenic, might be a *transient dweller* on the normal skin and various staphylococci streptococci diphtheroids, Candida species and some bacteria normally resident in the gastro-intestinal tract may frequently be discovered Such transient visitors are easier to remove by cleansing processes than are the resident organisms and the skin tends in any event, to quell them by its own anti microbic powers

The skin flora varies from one person to another and from one skin area to another and is influenced by environment, sweating infections elsewhere in the body and other factors. The lowest density of microbic population is on the non hairy trunk and the highest in the great folds in areas well supplied with sebaceous glands and in hairy areas To refrain from bathing does not markedly increase the bacterial population of the skin and any reduction in resident population produced by scrubbing is made up within about a week

scabies. Retro-auricular intertrigo blepharitis and angular stomatitis (perlèche) may be associated and regional lymph glands are often enlarged and may suppurate. Transient albuminuria may occur with widespread impetigo such as is seen as a complication of scabies.

In some cases the bullae do not rupture rapidly may be quite large and produce a pemphigus-like picture. Bullae of the periungual skin are not uncommon in children, but heal quickly with treatment so that loss of a nail is unusual. At other times the subcorneal exudation is minimal, but sufficient to loosen the stratum corneum so that spreading rings with scaling edges and very little scab formation or oozing of serum are seen. In many cases typical scabbed lesions, bullae and circinate scaly lesions coexist (Figs. 69 and 70).



FIG. 69

Circinate impetigo contagiosa.

[St. John's Hospital]

The diagnosis of primary impetigo presents little difficulty. Pustular and granulomatous secondary syphilides must always be remembered when dealing with impetigo in adults. Ringworm of the scalp in children may produce pustular lesions (kerion) but these are accompanied by falling of hair which does not occur in impetigo. Ringworm of the skin may resemble circinate impetigo but the lesions of the former are seldom so numerous and show tiny vesicles in their spreading edges.

Treatment. The vast majority of cases are quickly cured by the application of an antibiotic ointment such as aureomycin

It is due to infection with streptococci or staphylococci, is contagious and auto-inoculable and in children frequently occurs in little epidemics in schools or other institutions. Adults even those tending patients with impetigo are relatively rarely affected and experiments in passage of the disease are seldom successful no explanation for these phenomena is forthcoming

The lesions of impetigo are subcorneal vesicles or bullae arising rapidly on an erythematous base. If the bullae do not



Fig 68
Impetigo contagiosa.

quickly rupture the fluid becomes purulent, but early rupture is the rule and a soft honey-coloured scab forms (Fig 68) When this is removed a very superficial moist, red erosion is disclosed This heals leaving an erythematous or brownish macule that soon fades leaving no trace Untreated impetigo may last for many weeks extending as new lesions succeed the older ones. Large surfaces may be affected and confluence of lesions can produce big scabbed patches especially on the face Sites of election in primary impetigo are the face and the exposed skin of the hands arms and legs. Impetigo of the scalp often goes with head lice generalized impetigo with

during the earliest days of life on the palms and soles, arise from an indurated area of skin and are usually accompanied by other signs of syphilis.

Treatment The infant must be isolated and treated as for impetigo contagiosa with local and systemic antibiotics A daily bath in potassium permanganate solution should be given.

ECTHYMA

This is a variant of impetigo in which the infective process affects the dermis as well as the epidermis and leads to ulceration of the skin (Fig 71) It is commonly a primary



FIG. 71
Ecthyma.

phenomenon occurring at sites of minor trauma on the legs anterior surfaces) of children, but may occur in adults and as a complication of other diseases such as scabies. Malnutrition and debility are often associated The condition is often called by some local name, e.g veld sore or Natal sore in South Africa.

Ecthyma begins, like impetigo with a little bulla or pustule that is replaced by a thick adherent scab covering a

3 per cent thrice daily If crusting is so thick that the ointment alone will not soften it enough to allow easy removal starch poultices or soaking with olive oil may be used as well at first.



Fig 70
Confluent impetigo contagiosa.

Residual moist lesions or retro-auricular intertrigo may need the application of a lotion such as l eau Dalibour or 2 per cent eosin in 60 per cent alcohol Five per cent ammoniated mercury ointment or Quinolor ointment are used in the few cases resisting the antibiotics In rare cases of widespread impetigo in children it may be thought necessary to give systemic antibiotic treatment as well Penicillin and sulphonamides have no place in the treatment of impetigo because of their tendency to sensitize Precautions to avoid spread in a household must be taken

In impetigo secondary to scabies or pediculosis the primary condition must first be treated then the impetigo

IMPETIGO NEONATORUM

This is a form of bullous impetigo occurring usually in little epidemics in a hospital or institution and affecting infants between a few days and a year old The eruption may be localized or widespread and consists of tense bullae arising quickly on normal or erythematous skin The face is not often affected and the palms and soles very rarely Although the term pemphigus neonatorum is sometimes used for this disease it is unrelated to true pemphigus

Lesions appear in crops over a course of a few weeks, each element taking about a week to heal if untreated Septicaemia may occur and the condition is not one to be treated lightly Only bullous congenital syphilides are likely to have to be considered in differential diagnosis these commonly occur

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round torpid ulcer Around the ulcer the skin is slightly indurated and bluish One or many lesions may be present and the ulcers can be as large as 2 5 cm in diameter Healing leaves scars.

Differentiation from erythema induratum can be made sometimes only by biopsy

Treatment Ecthyma can be extremely stubborn especially in the winter months and may react very little to treatment with antibiotic ointments. If this is so the ulcer should be touched daily with 5 per cent silver nitrate solution and ringed with Lassar s paste. Occlusion with an Elastoplast or Viscopaste bandage is sometimes very useful in cases where the ulcers look clean but refuse to heal

BOCKHART S IMPETIGO

This is a superficial pustular perifolliculitis affecting usually the pilosebaceous follicles of the forearms, thighs and legs or scalp It may be an acute condition when most of the lesions are little pustules or chronic when pustules and red inflammatory papules are seen The treatment is that of impetigo contagiosa with antibiotic ointments etc

ECZEMATIDES

This term is often used particularly by the French dermatologists, for a still rather ill-defined group of coccal dermatoses characterized by scaling eczematous lesions. *Parakératoses* may be used in the same sense. In diseases of this group it is probable that the infecting organisms have allergenic powers as important as, if not more important than their pyogenic properties Some of these diseases are discussed under the headings of infective eczema *of adults and of children* and the lesions of seborrhoeic dermatitis are also related but occur on a particular terrain

A common eczematide affecting children and occasionally adults is *pityriasis streptogenes faciei* (pityriasis alba) The lesions are round or oval, pink or yellowish brown finely scaling patches usually on the face (particularly around the mouth) occasionally on the outer aspects of the deltoid areas of the arms and rarely elsewhere (Fig 72) The condition is

commonest in winter when the skin becomes chapped as a result of the cold and wind and is aggravated by over-use of



Fig 72
Pityriasis streptogenes faciei.

soap and water Untreated, the disease may last for months and often relapses each winter

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Wet dressings, poultices, and occlusive plasters should not be used as they make the skin sodden and allow infection to spread Squeezing the lesions may be dangerous especially when they are on the face (risk of sinus thrombosis and meningitis)

The treatment of chronic furunculosis is often disheartening The number of remedies suggested is large enough to show that there is no specific. The first step is to have the causative organism cultured and its sensitivity to the antibiotics determined so that the appropriate remedy may be tried, but the laboratory suggestions are not always successful in practice. A high protein, low carbohydrate diet and extra vitamins should be given.

HIDROSADENITIS SUPPURATIVA

This is a chronic, recurrent coccal infection of the axillary apocrine glands in adults. The lesions are red, tender nodules that often suppurate, discharge pus and leave chronic draining sinuses. Similar lesions are occasionally seen about the anus and buttocks, groins and genitals.

Treatment. Antibiotics are used in acute exacerbations, but if the disease becomes chronic and resistant, the best plan is to refer the patient to a plastic surgeon for excision of the area of gland-bearing skin and underlying necrotic tissue and grafting

ERYSIPELAS

Erysipelas is an acute febrile streptococcal infection of the skin that may seem to begin spontaneously but usually follows on trauma or develops from some pre-existing lesion such as a chronic ulcer (Fig 75) It has become quite rare in recent years, but was once common (e.g in surgical wards) and, before the days of sulphonamides and antibiotics of grave prognosis. The face and head are frequently affected, but any skin area and occasionally mucous surfaces may be involved. The patient often becomes seriously ill with high fever malaise and, sometimes, delirium or stupor Transient albuminuria is common and nephritis may follow an attack.

Erysipelas begins suddenly with a bright red, tense, shiny elevated rapidly-spreading plaque that in a few hours may

Treatment with an antibiotic or antibiotic hydrocortisone ointment is effective but cure may take several weeks.

In *Milian's trisymptomatic disease* which is probably due to streptococcal infection dyshidrosis is associated with an eruption of small round or oval scaly patches and plaques of erythroderma

Tinea amiantacea is probably also an eczematide This is a chronic dermatosis of the scalp in children characterized by patches of thick mica like scales that suggest a fungous infection It is very chronic and resistant to all forms of treatment but eventually clears entirely

Some cases of *érythrose péribuccale pigmentée* are eczematides and respond to antibiotics

FURUNCLE AND CARBUNCLE

A furuncle or boil is a deep necrosing folliculitis due to staphylococcal infection It begins with a superficial follicular pustule whose base becomes red painful and infiltrated to produce a deep-seated nodule. The pustule bursts and discharges a drop of pus and through the orifice so formed can be seen the dermal core of hard, yellow necrotic tissue which must be discharged or removed before healing with scarring can take place. Any part of the skin may be affected and there may be one or many lesions The term furunculosis is used for cases where boils persist in recurring over months or years diabetes may be a predisposing cause

A carbuncle is an agglomeration of furuncles affecting a small or large area of skin Multiple openings disclose the underlying necrotic tissue Pain and general symptoms are more important than with boils

Treatment The basic treatment for boils and carbuncles is rest, the application of dry heat by means of lamps or simply hot water bottles, and antibiotics locally or if necessary systemically Aureomycin may be used as an ointment or given orally penicillin may be used by injection. Surgical treatment is now seldom necessary but the core of necrotic tissue should be removed when it becomes loose Rarely a carbuncle fails to respond to antibiotics and continues to spread in such cases the process may be stopped by deep diathermy incision around the lesion and removal of necrotic tissue

negligible, but cases of erysipelas should never be nursed in surgical wards.

SYCOSIS AND FOLLICULITIS

The term sycosis should be reserved for chronic follicular (coccal) infections of the bristly haired areas, folliculitis for infections of other areas whether acute or chronic.

SYCOSIS BARBAE

Sycosis barbae is a common disease of the beard area in men that shows little tendency to spontaneous cure, may last for years and often recurs after apparent cure. It usually affects the whole bearded area, but sometimes is confined to the upper lip or to the beard margin on the neck. The lesions are little red, follicular papules or papulo-pustules often with excoriation and crusting, and the skin is generally erythematous (Fig 74) Nodules and lupoid papules are sometimes seen. The hairs may be easily and painlessly extractable, but they do not fall or break spontaneously Most cases probably begin as a banal impetigo or folliculitis that is spread and perpetuated by the trauma of shaving other cases, especially those on the upper lip, may be due to chronic intranasal infections. Friction from the collar is often a factor where lesions are localized to the neck.

Superficial scarring is seen in some cases and when this occurs a picture slightly suggestive of lupus vulgaris may be produced

The area involved is generally large and lesions are symmetrically distributed, points of distinction from the common form of trichophytosis of the face where the boggy nodular lesions are usually in relatively discrete plaques and often unilateral.

Treatment In a case of short duration 3 per cent aureomycin ointment rubbed well in thrice daily should first be tried If it is effective its use must be continued, after shaving for several weeks beyond the stage of apparent cure. If it is ineffective or if relapse occurs, treatment should be suspended for a few days, the organisms cultured and their sensitivity to antibiotics determined and the appropriate one substituted. In stubborn cases where a single remedy is only temporarily

cover a large area such as the whole face or scalp Loose skin such as that of the eyelids or genitals swells greatly Vesicles or bullae may appear and, at a later stage, abscess formation or even gangrene of the skin Regional lymph glands are enlarged and may suppurate

In an untreated case spread continues for several days and then provided the forces of immunity come into play the



FIG 73
Erysipelas around a chronic ulcer

oedema begins to subside, the colour changes to brownish yellow and the epithelium scales off

*Subacute recurrent forms of erysipelas are also en*countered and in such cases elephantiasic swelling of the face genitals or a limb may result

Treatment The prognosis of erysipelas is now good and fatalities are rare save in infants or debilitated elderly people. Penicillin and the other antibiotics given at once in the early stages rapidly cure the disease sulphonamides are less quickly effective Rest in bed is usually indicated and simple soothing lotions may be applied The risk of contagion to attendants is

effective success may follow the use of an antibiotic ointment, Quinolor ointment and 5 per cent ammoniated mercury ointment week about. Before the days of antibiotics Quinolor was the best remedy available. Antibiotic-hydrocortisone ointments are sometimes effective.

The factor of pure trauma in shaving, quite apart from autoinoculation, is important, and the use of an electric shaver is of great value in difficult cases. Where chronic nasal infection is involved this must obviously be treated.

SYCOSIS NUCHAE

Sycosis nuchae, also known as dermatitis papillaris capillitii or acne keloid, is a chronic follicular infection of the

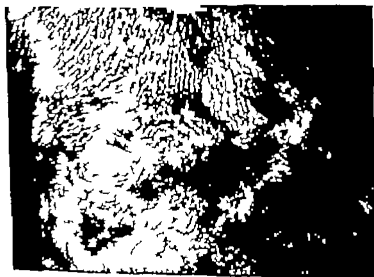


FIG 75
Sycosis nuchae.

nape of the neck and occipital scalp in men. It often begins in adolescence and may persist for many years. It may be a solitary phenomenon or appear as part of a severe acne vulgaris in which case large cysts and abscesses may be associated (Figs. 75 and 76)

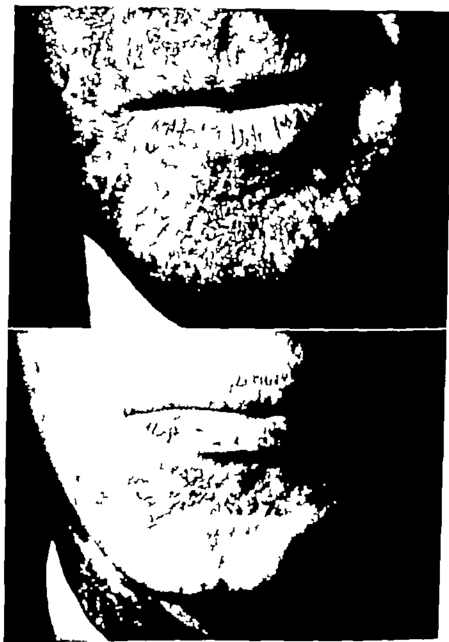


Fig. 74.
Sycosis barbae
Top Follicular *Bottom*. Lupoid

(Fig 77) It is one of the varieties of pseudo-pelade Favus must be remembered in differential diagnosis.

Treatment is as for sycosis barbae, but the disease usually proves extremely stubborn



Fig. 77
Folliculitis decalvans.

([illegible])

FOLLICULITIS ABSCEDENS ET SUFFODIENS

This is a rare condition of the scalp characterized by multiple indolent abscesses starting in large comedos and leading to scarring and alopecia.

Treatment is by minor surgery and appropriate antibiotics locally and systemically

ACNE NECROTICA

Acne necrotica is chronic folliculitis affecting the scalp and adjacent temples and forehead in adults Seborrhoeic subjects are particularly prone to be affected. The lesions are red, itchy and painful papules with a central black, adherent

The lesions are follicular papules and pustules that constantly recur and often lead to patchy alopecia and multiple small round nodular keloidal scars

Treatment as for sycosis barbae may help in the early stages or be of sufficient benefit to help the patient through



Fig 76

Sycosis nuchae Final stage of keloidal scarring

[St John Hospital]

bursts of activity In the type associated with deep abscesses plastic surgery gives the best results

Sycosis of other areas Sycosis of the eyebrows or of the pubic area is *sometimes seen and is treated in the same way as* sycosis barbae A background of seborrhoea is commonly found

FOLLICULITIS DECALVANS

This is a *chronic, spreading sycosis of the scalp* In an established case follicular pustules are seen at the edge of a scarred bald area in which a few odd hairs are still present

Treatment with antibiotic ointments helps to subdue an attack, but recurrence is to be expected

OTHER TYPES OF FOLLICULITIS

Although folliculitis is commonest in areas with bristly hairs, coccal infections of follicles on glabrous skin are not rare. Some people are very prone to folliculitis and nobody goes through life without suffering from one or other of its manifestations. The beard area, the nape of the neck, the outer sides of the thighs, the nostrils and eyelids (styes) are sites of election, doubtless as a result of their liability to be rubbed and otherwise injured

Folliculitis often develops round boils or other infected lesions especially when fomentations, poultices and adhesive, occlusive dressings are applied. Pustular lesions complicate oil or chlorine acne and sometimes arise after the use of mercury or tar ointment on hairy areas. Bockhart's impetigo is a variety of folliculitis. Most cases of folliculitis clear up rapidly with antibiotic ointments and the removal of any source of irritation (e.g by using an electric instead of a blade razor)

INTERTRIGO

Inflammation of skin folds such as those of the axillae and groins, and of the retro-auricular submammary umbilical and interdigital areas is often due to streptococcal infection (Fig 79) The skin is red and glazed and may also show scaling vesicles and pustules. Obese people are oftenest affected and predisposing factors are lack of hygiene and diabetes.

Treatment consists in keeping the skin clean and dry and applying lotions such as Castellani's paint or 2 per cent eosin in 60 per cent alcohol and a simple talcum powder Antibiotics may be necessary at first.

ACRODERMATITIS CONTINUA (HALLOPEAU)

This disease, which is also known as acrodermatitis perstans or dermatitis repens, begins on a finger often near the nail, as a vesicular eruption on red, slightly oedematous, scaling skin. The lesions slowly spread and other fingers on the same and the other hand may later suffer Transverse or

crust, that heal slowly and often leave scars the hair follicle is destroyed in the process Papulo-necrotic tuberculide is closely simulated and it is probable that the necrosis is due to sensitization to the infecting cocci In rare cases the distribution

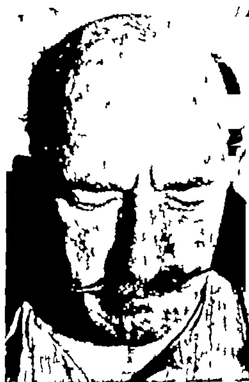


FIG. 78

Acne necrotica.

[St John's Hospital]

of the disease is wider and similar lesions may be seen on the trunk or limbs (Fig 78)

Treatment is generally unsatisfactory Antibiotic or antibiotic hydrocortisone ointments or lotions may be effective and some successes are obtained with systemic antihistaminics or corticosteroids and local antibiotics

FOLLICULITIS PENETRANS NASI

This is a chronic recurrent infection of the follicle of one of the nasal vibrissae at the nose tip within the nostril producing a very painful furunculoid swelling

Acrodermatitis continua is a diagnosis of elimination used for chronic vesiculo-pustular eruptions of the extremities of unproved origin.

Treatment. Antibiotic ointments alone or with hydrocortisone may help mercury and tar ointments can be tried.



Fig. 80

Acrodermatitis continua (Hallopeau)

(Annales de Dermatologie et de Syphiligraphie)

GRANULOMA PYOGENICUM

Granuloma pyogenicum, or botriomycoma, appears as a solitary growth in the majority of cases at the site of some minor injury to the skin, scalp lips or buccal mucosa. The hands and face are oftenest affected The lesion is a sessile

vertical striations or pitting of the nails may occur The evolution is extremely chronic with remissions and relapses and spread to the palms may eventually take place. Activity is greatest in the edges of the lesions but complete healing does not take place in the central areas A pustular form is also



Fig 79
Intertrigo due t coccal infection

described in which loss of nails may occur and where lesions may appear in areas far removed from the hands (Fig 80)

It is debatable whether these pictures are always produced by the same cause but the rapid clearing of lesions after the use of modern antibiotic ointments suggests that some at least are due to chronic pyogenic infection Psoriasis in its pustular form may long remain localized to the hands and feet and give just such an appearance The name pustular bacteride has been given to cases of chronic vesiculo-pustular eruptions that often begin in the middle of the palms and soles and are thought to be bacterial allergides, reactions to bacteria disseminated from some chronic source of infection in teeth tonsils, etc.

Acrodermatitis continua is a diagnosis of elimination used for chronic vesiculo-pustular eruptions of the extremities of unproved origin.

Treatment Antibiotic ointments alone or with hydrocortisone may help mercury and tar ointments can be tried.



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or pedunculated tumour up to about 1 cm in diameter in most cases, occasionally larger (Fig 81) It is red in colour and covered by a thin shiny epithelium that is easily broken to allow free bleeding Full size is reached in a few weeks and then the tumour shows no tendency to enlarge or to disappear

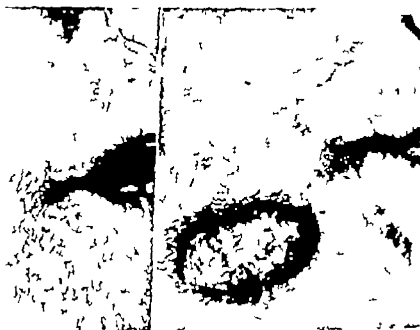


Fig. 81
Granuloma pyogenicum.

Histopathology Under a flattened epithelium are dilated new formed capillaries embedded in loose oedematous connective tissue and a variable amount of inflammatory cells. The picture is that of a capillary haemangioma and there is some discussion as to the role played by pyogenic organisms in the cause of this growth

Treatment The only sure way of cure is to destroy the tumour and its base with the diathermy

VEGETATING AND VERRUCOUS PYODERMAS

Vegetating or verrucous lesions may develop on impetiginous ecthymatous or impetiginized conditions or they may develop *de novo*

Fetid, oozing vegetating lesions are oftenest seen in the large skin folds and round the natural orifices and may produce a picture suggestive of syphilis, tuberculosis or some deep mycosis. States of malnutrition (e.g. pellagra) and debility as well as lack of hygiene predispose to their appearance.



Fig. 82
Vegetating pyoderma

Chronic verrucous lesions resembling those of verrucous tuberculosis or chromoblastomycosis may be seen on the hands, wrists and forearms. Pseudo-epitheliomatous hyperplasia of the epidermis may be a feature of the histological picture (Fig. 82).

Treatment is with antibiotics and drying lotions and powders for the moist lesions Verrucous lesions often have to be removed with the diathermy

PYODERMATITIS VEGETANS OF HALLOPEAU

This is a rare disease easily confused with pemphigus vegetans, which is characterized by large plaques of elevated,



FIG. 83
Pyodermatitis vegetans of Hallopeau
[K Degos]

reddish brown scaling itchy skin that result from the aggregation of many small vesiculo-pustules Vast areas may be covered and the scalp chest and back and great folds are usually affected After a few months of rapid progress the disease settles into a chronic state (Fig 83)

Histopathology There is considerable acanthosis with little abscesses full of polymorphonuclear leukocytes in the inter papillary processes.

Treatment is with potassium permanganate baths and local and systemic antibiotics.

SOLITARY CHANCRIFORM PYODERMA

This is a rare condition in which a pustule develops into a scabbed ulcer with a firm, indurated base, that is clinically indistinguishable from a syphilitic chancre The face and genitals are sites of election. Regional glands are enlarged and tender and may suppurate. Syphilis must be excluded by repeated dark-ground and serum tests. Antibiotic ointments are used in treatment.

GANGRENOUS PYODERMAS

A variety of skin conditions are described in which gangrene is part of the picture and where pyogenic infections are known or suspected as causes. Gangrenous lesions may supervene in other infective conditions, as for example in acne conglobata, or they may arise *de novo* they may be acute, fulminating and grave, or they may be chronic.

PYODERMA CHRONICA PAPILLARIS ET EXULCERANS

This disease is characterized by multiple papillary granulomatous, ulcerative and gangrenous, slowly-spreading, serpiginous lesions that resemble closely those of blastomycosis (the disease has been called pseudo-blastomycosis) Healing is slow leaves scars, and fresh lesions continue to appear over years. No specific treatment is known, but one case healed rapidly while on antibiotics and cortisone

POSTOPERATIVE PROGRESSIVE BACTERIAL SYNERGISTIC GANGRENE (MELENEY'S ULCER)

Meleney's ulcer usually begins around some surgical drainage wound and consists of a slowly spreading area of necrosis surrounded by an inner zone of purplish skin and an outer red zone. Spread may continue for many months. This condition is believed to be caused by a microaerophilic

Treatment is with antibiotics and drying lotions and powders for the moist lesions Verrucous lesions often have to be removed with the diathermy

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Treatment is with potassium permanganate baths and local and systemic antibiotics

Solitary chancriform pyoderma

This is a rare condition in which a pustule develops into a scabbed ulcer with a firm, indurated base, that is clinically undistinguishable from a syphilitic chancre. The face and genitals are sites of election. Regional glands are enlarged and tender and may suppurate. Syphilis must be excluded by repeated dark-ground and serum tests. Antibiotic ointments are used in treatment.

Gangrenous pyodermas

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Pyoderma chronica papillaris et exulcerans

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Postoperative progressive bacterial synergistic gangrene (Meleney's ulcer)

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Treatment is with antibiotics and drying lotions and powders for the moist lesions Verrucous lesions often have to be removed with the diathermy

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Fig. 83

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[E Dyer

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or the cachectic or it may be a very chronic recurrent condition that has oddly little effect on general health In one case the disease persisted over twelve years until the patient's death from pneumonia and eventually scarred all the body surface except the face (Fig 84) The cause is unknown but the lesions bear a striking resemblance to those of the post operative gangrene described above and can be halted by cutting around with the diathermy Antibiotics plus corticosteroids should obviously be tried in such cases.

MULTIPLE GANGRENE OF CHILDREN

This condition may develop in the course of varicella or other infectious fevers or appear seemingly without reason. Acute and fatal and benign varieties are seen. In cases not responding to antibiotics alone it would be worth while trying the effect of adding corticosteroids.

GANGRENE OF THE GENITALS

Gangrene may result from secondary infections in cases of genital ulceration (especially in men) due to syphilis, chancroid, etc.

Fulminating gangrene of the penis begins suddenly with a red hard oedema of the skin which soon becomes gangrenous. The area affected may be quite localized or large, spreading and mutilating in which case it may be fatal. I have seen two cases, both in men suffering from pneumonia in the days before antibiotics In one the prepuce was neatly removed by the process and the patient recovered, but the other was rapidly spreading and fatal

GONORRHOEA

Cutaneous lesions were never common in gonorrhoea and have become exceptionally rare since the advent of penicillin which usually cures the disease in a very short time and prevents the development of the chronic, focal complications that are often responsible for the development of skin lesions.

Ulcers or erosions of the genital mucosa or adjacent skin caused by gonococcal infection are occasionally seen in typical gonorrhoea and very rarely indeed may be primary phenomena.

non haemolytic streptococcus in the spreading edge and a staphylococcus in the gangrenous area

Treatment usually consists in cutting with the diathermy a deep firebreak around the edge in normal skin Antibiotics alone are almost invariably ineffective but antibiotics plus corticosteroids may cause rapid cure in the most chronic cases and should now be the first method used

Similar spreading ulcerative lesions of the legs or trunk, starting on apparently normal skin are occasionally seen in cases of ulcerative colitis. Fresh lesions appear during exacerbations of the colitis and the two conditions wax and wane together

MULTIPLE GANGRENE OF ADULTS

In this condition are seen multiple spreading areas of gangrene beginning sometimes as little abscesses, sometimes



FIG. 84
Multiple gangrene of adults.

appearing quite suddenly in hitherto normal skin It may be a fulminating and fatal disease in old people the debilitated

Infections of Tyson's parafrenal glands or abnormal skin or mucosal indentations come into this category

Simple erythema may occur in untreated acute gonorrhoea and urticarial, papular or even purpuric rashes, allergides, with gonococcal arthritis. Purpuric, bullous and pustular eruptions and subcutaneous abscesses may occur with gonococcal septicaemia and subacute bacterial endocarditis.

Keratoderma blenorrhagica is the most interesting of the skin manifestations occurring with gonorrhoea, usually in cases with arthritis. Some observers claim to have found gonococci in the lesions, but the same eruption may be found in Reiter's syndrome and there is some dispute as to whether this keratosis is due to gonococcal infection or to a coincidental infection with the as yet undiscovered cause of Reiter's syndrome. The lesions are originally deep vesiculo-pustules that soon are covered by thick adherent scales and become aggregated into rupial corns, crusts or small plaques (Fig 85) The soles are oftenest affected, but lesions may also arise on the legs, palms and arms and occasionally elsewhere. Psoriasis is simulated and Millian even suggested that the condition was psoriasis precipitated by gonorrhoea. With these lesions, or sometimes alone, occurs a circinate balanitis with red rings covered over or at the edges with heaped-up dry or macerated epithelium. Subungual hyperkeratosis and deformation and even shedding of nails occur in some cases.

Treatment Penicillin is the basic remedy for gonorrhoea and all its complications, but any of the antibiotics will give equally good results in patients allergic to penicillin. The duration of antibiotic treatment depends on the gravity of the complication and local treatment may still be necessary for focal infections in the prostate, Fallopian tubes, etc. Keratoderma is treated with keratolytics such as 4 to 10 per cent salicylic acid ointment or Whitfield's ointment.

REITER'S SYNDROME

The cause of this condition is unknown (it is suspected to be a micro-organism) and it is considered here because of the similarity of its lesions to some of those of gonorrhoea. The manifestations are chronic urethritis, conjunctivitis, polyarthritis and an eruption identical with keratoderma

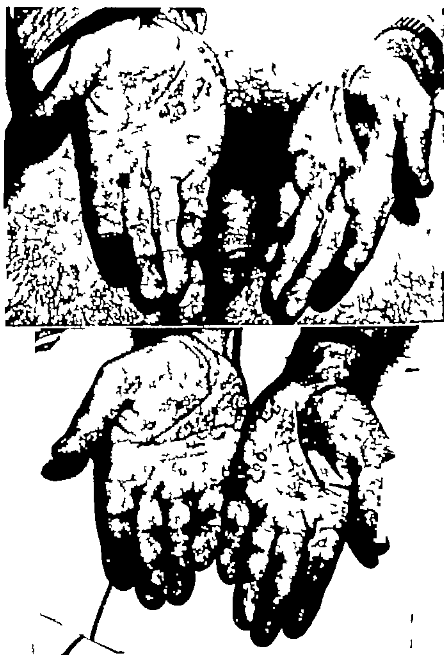


Fig 83

Keratoderma blennorrhagica. Early vesiculo-pustular lesions become squamous and keratotic.

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blennorrhagica It is a febrile debilitating illness that lasts for months or even a year or more It may relapse after apparent cure but eventually goes on to complete recovery (Fig 86)

The conjunctivo-urethro-synovial syndrome of Fiessinger and Leroy which is associated with pseudo-dysenteric symptoms is probably identical with Reiter's syndrome



Fig 86

Reiter syndrome Arthritis, keratosis and nail changes.

(Courtesy of Cape Town (left))

Treatment The antibiotics usually have little or no effect on any of the symptoms but the arthritis can be controlled with ACTH or corticosteroids

SOME BACILLARY INFECTIONS

ANTHRAX

Anthrax, or malignant pustule, is a grave acute infection caused by *Bacillus anthracis*. Primarily a disease of animals (sheep, goats, horses, cattle) it is in man almost always an occupational disease of farmers, tanners, hide porters, butchers or wool-sorters. The anthrax bacillus is very resistant and persists almost indefinitely in infected tissues. Cutaneous infections are commonest but intestinal and pulmonary forms of the disease, usually fatal, occur after ingestion or inhalation of infected material.



Fig. 87
Anthrax treated with neo-arsphenamine
(D. R. Pinder)

Skin lesions, often solitary and seldom numerous, appear 2 to 5 days after inoculation, usually on the exposed skin of the face, hands or arms (Figs. 87 and 88). The first sign is a red patch like an insect bite on which develops a sero-haemorrhagic vesicle. This ruptures to disclose a patch of black necrotic tissue; around this is a red areola of indurated skin studded with vesicles. The lesion spreads rapidly and is accompanied by varying degrees of tissue oedema, which in its most prominent form, is known as malignant oedema. Regional glands are enlarged and tender and signs of septicaemia often appear. In untreated cases death follows in about 7 to 10 days, less in malignant oedema; spontaneous cure is rare.

Furuncles, erysipelas and insect bites may cause confusion in diagnosis which is established by demonstration of the

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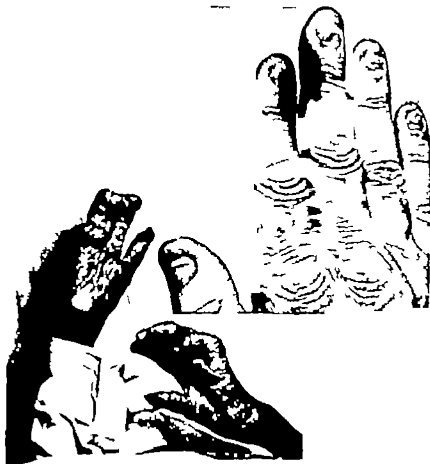


Fig 86

Reiter syndrome Arthritis, keratosis and nail changes.

(Courtesy of [illegible])

Treatment The antibiotics usually have little or no effect on any of the symptoms, but the arthritis can be controlled with ACTH or corticosteroids

ulcerate The respiratory mucosa is often first affected and multilating ulcers of the nose and face develop The chronic form may last for many months before a terminal acute exacerbation.

The causative organism can be demonstrated by direct examination, culture and animal inoculation



FIG. 89
Glanders

London Hospital

Treatment is not very successful. The primary lesion may be excised with the diathermy Antibiotics and sulphonamides should be tried Vaccinotherapy with mallein and anti-glanders serum have been used in chronic cases.

MELIOIDOSIS

This is a disease of rodents rarely communicated to man where it causes a picture like that of glanders. The cause is *Malleomyces pseudomallei*. Cases have been reported in the Rangoon area and occasionally elsewhere. Excision and sulphadiazine are recommended.

ERYSIPELOID

Erysipeloid is a fairly common condition due to infection with *Erysipelothrix rhusiopathiae* the cause of swine erysipelas. Th organism is widely distributed in nature mainly on

organism in smears and cultures from local material by blood culture and by animal inoculation

Treatment Early treatment with penicillin and sulphadiazine gives excellent results and has largely superseded the use of arsphenamines or anti-serum which is seldom immediately available



Fig 88

Anthrax. His pig died so he quickly [illegible] it.

[[illegible]]

Glanders

Glanders farcy or equinia is a disease of horses mules and donkeys *transmissable to man and caused by Malleomyces mallei* The disease is usually seen in people who handle horses or in those engaged in the preparation of mallein

An acute form may be primary or terminal It is characterized by septicaemia, lymphangitis, erysipelas-like engorgement of the face multiple exuberant abscesses and lesions of the mucosa of the nose mouth and pharynx This is fatal in a few weeks

In the chronic form, the primary lesion is a papulo-pustule that develops *into a deep spreading ulcer* (Fig 89) Nodules (farcy buds) develop in the line of the lymphatics and also

RHINOSCLEROMA

Rhinoscleroma is a chronic granulomatous disease that affects the nose, sinuses, pharynx, larynx, trachea and bronchi. The causative organism is *Klebsiella rhinoscleromatis* (Frisch bacillus). It occurs particularly in Central and Eastern Europe, Central America and Indonesia, but cases usually imported, have been reported from most parts of the world.

The disease begins usually in the nose as a submucous infiltrating granuloma. Nodules, polypi and diffuse infiltrates are seen and in time may produce gross swellings and mutilations of the nose and face. Deformity may be worsened by eventual fibrosis. Symptoms include nasal obstruction, hoarseness and coughing, dysphagia, deafness and difficulty in speech. Death often occurred in the past from respiratory obstruction and secondary infections.

In established cases Mikulicz cells, large histiocytes with foamy cytoplasm and pyknotic nucleus, containing rod-like bacilli are seen in the tissues. Russell bodies, round or oval PAS-positive hyaline masses, are seen free or within plasma cells which are generally numerous.

Treatment is by surgical excision, where possible, and antibiotics. The organism is sensitive to streptomycin, aureomycin, terramycin and chloromycetin.

CHANCROID

Chancroid, ulcus molle or soft chancre, is a common venereal disease caused by Ducrey's bacillus *Haemophilus Ducreyi*. Its distribution is world wide but it is commoner in warm climates than in cold. The vast majority of cases are seen in men and it is probable that women are usually asymptomatic carriers. The genitals are usually affected and extra-genital lesions are very rare (Fig. 90). The incubation period is 1 to 8 days.

The lesions of chancroid are usually multiple from the start or increase in numbers by auto-inoculation. They are little deep, tender ulcers, irregular in shape with a yellow necrotic base and surrounded by oedematous, inflamed skin. The edge of the prepuce is a common site fo such ulcers and festering fissures. Inguinal adenopathy is common and often

dead animal and vegetable matter and most cases in man are seen in butchers slaughterers cooks poultry farmers etc

The lesion (there is very rarely more than one) is usually on the fingers or hand and *arises a few days after some cut or scratch* It is a slowly spreading patch of slightly-elevated, tense tender reddish blue skin in which the primary injury may still be visible Large areas are rarely involved by spread and a patch on a hand seldom goes beyond the wrist Spontaneous cure takes *place in a few weeks to 2 or 3* months

Complications are rare but periarthritis and arthritis, lymphangitis and adenopathy diffuse and generalized erythematous patchy eruptions and septicaemia with purpuric lesions and endocarditis have been noted

Treatment Penicillin and other antibiotics and sulphonamides all have some effect on erysipeloid but seldom produce spectacularly speedy cure Recurrence *in situ* and reinfection are possible

Diphtheria

Infection of the skin with *Corynebacterium diphtheriae* can *produce a great variety of lesions of an acute or chronic nature* which are by no means always associated with the usual mucosal lesions All the complications of diphtheria may occur and fatalities are not uncommon since the nature of the infection may long go unrecognized Skin diphtheria some*times seems to be a primary infection* but usually it is superimposed on a wound or on an existing skin eruption and the lesions may be localized or generalized

Grey membranous ulcers, necrotic ulcers, vesicular pustular and bullous eruptions are all described Lesions resembling those of ecthyma are not uncommon Varicelliform rashes like those of Kaposi s varicelliform eruption have been seen During an epidemic outbreak in a skin ward I saw two cases *with penile lesions clinically indistinguishable* from syphilitic chancres

Treatment Patients must be quarantined and treated with antitoxin and antibiotics Ecthymatous lesions may be very slow to heal

remedy which is ineffective against syphilis. Sulphadiazine, 1 g four times daily for 7 to 10 days, or streptomycin 1 g daily until the lesions are healed, are the drugs of choice and will not interfere with dark-ground examinations which must



FIG. 9

Chancroid. *Top*: Buboes. *Bottom*: Ulcus molle serpiginosum.

be done daily for several days as a first step to exclude syphilis. Saline soaks or dressings are the only local applications permissible or required at this stage. Syphilis may develop later at the chancroid sites or elsewhere if the two diseases have been inoculated at the same time. Penicillin in doses not less than

goes on to suppuration, ulceration may begin in the overlying skin when an abscess points and spread to produce ulcus molle serpiginosum (Fig 91)

Chancroid may be quite destructive and eat away the frenum (causing sharp haemorrhage) or perforate the prepuce. Phagedenic ulcers as a result of added fuso-spirochaetal infections may be mutilating Little abscesses, chancroidal



Fig. 90
Chancroid

[H B Sawers (right)] [R. Degos (left)]

bubonuli may appear along the shaft of the penis in the line of the dorsal lymphatics

Direct diagnostic methods such as the demonstration of Ducrey's bacillus in material from lesions, auto-inoculation experiments and the Ito-Reenstierna intradermal test with Dmelcos vaccine are mainly of academic interest Any *genital sore should be suspected of being syphilitic until proved* otherwise and although a presumptive diagnosis of chancroid may be made at once, a positive diagnosis is made in retrospect when syphilis is excluded by follow up serum tests over three months

Treatment The sulphonamides and most of the antibiotics are effective against chancroid but because it is difficult to distinguish clinically between chancroid and syphilis and because the two diseases may coexist, it is wise to choose a

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FIG. 91

Chancroid *Top*, Buboes *Bottom* Ulcus molle serpiginosum.

ad L. Murray

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Fig. 90
Chancroid

[R. Degos (left)]
[H W Siemens (right)]

bubonuli may appear along the shaft of the penis in the line of the dorsal lymphatics.

Direct diagnostic methods such as the demonstration of Ducrey's bacillus in material from lesions, auto-inoculation experiments and the Ito-Reenstierna intradermal test with Dmelcos vaccine are mainly of academic interest. Any genital sore should be suspected of being syphilitic until proved otherwise and although a presumptive diagnosis of chancroid may be made at once, a *positive diagnosis is made in retrospect* when syphilis is excluded by follow up serum tests over three months

Treatment The sulphonamides and most of the antibiotics are effective against chancroid but because it is difficult to distinguish clinically between chancroid and syphilis and because the two diseases may coexist, it is wise to choose a

Treatment. Streptomycin, 2 g daily for a week, is reported to be very effective in all types.

BALANO-POSTHITIS

Balano-posthitis, commonly referred to as balanitis, is an inflammation of the glans penis and inner surface of the prepuce that may occur alone or with venereal diseases, especially gonorrhoea. Fusiform bacilli and spirochaetes (not *T pallidum*) are usually present in the lesions, but it is not known whether they are causative or simply saprophytic. Balanitis is seen especially in unhygienic men with long tight foreskins.

The inflammation may be mild and cause only superficial often circinate, erosions or severe with oedema, loss of all the epithelium and, frequently phimosis or paraphimosis. Gangrenous balanitis, phagedena, is rare but very destructive

In cases with phimosis where the prepuce cannot be retracted, gonorrhoea may be simulated. The erosions may closely resemble th lesions of primary and secondary syphilis and it must be remembered that primary syphilis may present as an erosive balanitis (Follmann's balanitis) Balanitis is a common feature of Reiter's syndrome

Treatment. Bathing and, if necessary subpreputial syringing with warm saline or potassium permanganate solution is all that is required in most cases. Wiping over with methylated spirits is a painful but effective method of drying the lesions and may be followed by th application of talcum powder Ointments should not be used as they usually aggravate the condition. In all but the most obvious cases dark-ground and serum tests (over three months) for syphilis will be required Penicillin by injection is used for gangrenous balanitis. Where balanitis recurs frequently it is often necessary to circumcise

GRANULOMA INGUINALE

Granuloma inguinale (G venereum, Donovanosis) is a disease characterized by granulating lesions of the genital area. It is probably often, if not always, a venereal disease. The causative organism *Donovania granulomatis* is provisionally classified as a bacterium. Cases have been seen all over the

those used for primary syphilis (6 000 000 units) are used for phagedenic chancroid this is also suggested for the treatment of genital ulcers in backward areas where both diseases are common and it is unlikely that cases will attend for follow-up examinations

Tularemia

Tularemia is a febrile disease caused by *Pasteurella tularensis* which may be communicated to man by contact with infected animals (wild rabbits particularly) or through fly or tick bites The disease is commonest in the western and southern United States and shows a variety of clinical pictures all characterized by sudden onset with fever chills, headache general malaise and often gastro-intestinal symptoms after an incubation period of 2 to 7 days.



Fig 92
Tularemia Ulcer site of inoculation.
[*John D Kirschbaum*]

The ulcero glandular type begins with a papular or nodular lesion on exposed skin or conjunctiva that breaks down to form a necrotic ulcer about 1 cm. in diameter (Fig 92) Lymphangitis follows and the lymph glands enlarge and often suppurate to produce a picture like that seen in sporotrichosis which is distinguished by the absence of symptoms and slower progress. Generalized erythema multiforme-like eruptions and herpetiform and localized pustular rashes occur in some cases.

In the oculo-glandular type the primary lesion is a conjunctivitis with regional adenitis Sometimes a set of glands will enlarge without evidence of an inoculation site Typhoid pulmonary and meningeal syndromes also occur

tropical belt and it is fairly common in the United States, particularly in the South, where negroes are far oftener affected than whites. Men are twice as susceptible as women The disease is apparently not highly contagious.

The primary lesion, which appears after an incubation period averaging fifteen days, is an indurated papule that becomes eroded and forms a slowly-spreading ulcer with a beefy granulating base and markedly raised, velvety granulations at the edge (Fig 93) Vast areas of the genital, pubic and anal skin may be destroyed as spread proceeds with new lesions beyond the advancing edge gradually being included. There is little tendency to spontaneous healing The cervix uteri may be affected and inguinal glands may enlarge, break down, and produce new lesions in the skin. Arrest may take place at any stage or great spread and secondary fuso-spirochaetal infection may lead to cachexia and death Metastatic lesions may appear in bones and distant lymph glands. Keloidal scarring, elephantiasis and malignant changes may occur Extragenital infections are uncommon.

The disease is distinguished from other granulomatous diseases of the genital area by tests of exclusion and by demonstrating the causative organism in biopsy material or in tissue scrapings. A complement-fixation test can also be done.

Histopathology The epidermis may be thinned or show pseudo-epitheliomatous hyperplasia. A dermal infiltrate consists predominantly of histiocytes and plasma cells with scattered small abscesses composed of polymorphonuclear leukocytes lymphocytes are conspicuously rare. Within some large histiocytes inclusion (Donovan) bodies are seen as groups of small round or oval, encapsulated particles these stain red with Giemsa's stain and are most easily demonstrable in scrapings.

Treatment Streptomycin, 4 g daily for five days, is very effective even in chronic cases. Aureomycin, terramycin and chloromycetin can also be used with good results, but penicillin is effective only against secondary infections. Surgery may be necessary to correct mutilations. The antimonials (e.g Fouadin) have largely been abandoned except in cases resisting antibiotic therapy



FIG. 93

Granuloma inguinale

[K. O'Mallon
R. R. Illiam]

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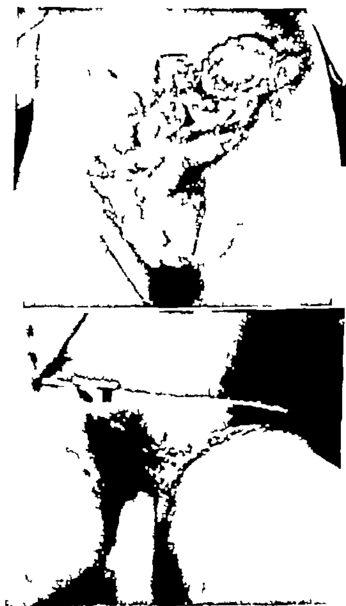


FIG. 93
Granuloma inguinal

[C. A. O'Malley
R. R. Wallace]

two diseases and one hesitates to propose any direct causal relationship.

ERYTHEMA CHRONICUM MIGRANS

The first sign of disease is a red infiltrated papule or little plaque. Peripheral spread and central healing, without atrophy, produces a continuous or broken ring with a dusky-red, infiltrated border 5 to 20 mm in width (Fig. 94). Very



FIG. 94
Erythema chronicum migrans

large areas may be included within the advancing edge, but eventually, after a few months to a year, the lesions heal and leave no trace. A solitary lesion is the rule and there are never more than a few. Sites of election are the legs, but any area may be involved. Traces of tick bites may be found; the delay between bite and appearance of lesions varies between two weeks and four months.

The general health is usually unaffected, but febrile forms occur and cases with monocytic or leukocytic meningeal reactions, radiculitis and even encephalitis have been reported. The changes in the skin are non-specific, with a dermal infiltrate consisting largely of lymphocytes.

Treatment with penicillin and other antibiotics is rapidly curative in both simple and complicated cases.

SOME DISEASES PROBABLY DUE TO INFECTION

The diseases discussed in the following pages are included in this chapter because there is some evidence to show that they may be caused by microbic infection

ACRODERMATITIS CHRONICA ATROPHICANS (PICK HERXHEIMER) AND ERYTHEMA CHRONICUM MIGRANS (AFZELIUS-LIPSCHÜTZ)

Acrodermatitis chronica atrophicans is a relatively common disease in Central Northern and Eastern Europe. *Elsewhere it is rare and many of the cases reported from other* lands have occurred in immigrants from the endemic areas. Although the geographical distribution of erythema chronicum migrans has not received any special study case reports in the literature suggest that it is roughly the same The region indicated lies within the area of distribution of the tick *Ixodes ricinus* and a history of tick bites preceding the onset of symptoms is often given by patients with both these diseases *Ixodes ricinus* has frequently been implicated in those cases of erythema chronicum migrans which have been carefully investigated Both the diseases have been successfully reproduced in man by subcutaneous implantation of skin fragments from affected patients suggesting that they are infective in origin *The fact that both respond rapidly to treatment* with antibiotics supports the theory of infection

Acrodermatitis chronica atrophicans and erythema chronicum migrans may coexist on the same patient and the early lesions of the former may closely resemble those of the latter It is probable that the two conditions are caused by the same tick borne infective agent and that erythema chronicum migrans may be taken as the basic acute lesion *which* may proceed either to spontaneous (or therapeutic) cure or to a chronic stage represented by acrodermatitis chronica *atrophicans*

Lesions of lymphadenosis benigna cutis (localized form) may be found in patients with either condition This disease, has been reproduced in passage experiments in man, but its geographical distribution its resistance to antibiotics and the sites of election for its lesions are not like those of the other

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are visible through the epidermis. Bands of scleroderma-like fibrosis may be seen especially in ulnar or tibial distribution and gaiter like sclerosis of the lower third of the leg is described. Macular atrophy (anetoderma) poikiloderma, striate atrophy patchy hyperpigmentation, varices and leg ulcers may also arise. Atrophic lesions of the buccal laryngeal and genital mucous membranes have rarely been noted. In the stage of onset and spread the skin is usually itchy and then hyperaesthetic. The underlying bones are tender to pressure and the joints may be stiff

The lesions may continue to spread for many years, but eventually become inactive The general health is unaffected and although the erythrocyte sedimentation rate may be increased there are no constant or characteristic changes in the blood or marrow Squamous-cell carcinoma and sarcoma have been reported to develop on the lesions.

The clinical picture in the late phase is so striking that the diagnosis is usually obvious. In rare cases where confusion with scleroderma, poikiloderma or senile atrophy might arise the problem is solved by histological examination.

Histopathology In the early stage there is an important dermal, particularly perivascular infiltrate of lymphocytes, plasmocytes, histiocytes and fibrocytes. Telangiectatic vessels with thickened walls and sometimes thromboses are a prominent feature There is dermal oedema with hyaline degeneration of the collagen fibres and fragmentation of the lastic fibres.

The epidermis is a little hyperkeratotic and slowly trophies until, finally it consists of only a few layers of cells. In the late stages there is dermal atrophy disappearance of infiltrate increased fragmentation of elastic tissue and, eventually disappearance of hair follicles and sebaceous glands the blood vessels remain dilated

Treatment with penicillin or any other antibiotic arrests the disease at any stage but naturally has no effect on established, atrophic lesions.

ACRODERMATITIS ENTEROPATHICA

Acrodermatitis enteropathica is a rare disease often familial, that begins in infancy and is usually fully developed

ACRODERMATITIS CHRONICA ATROPHICANS

The name is rather misleading as the actual extremities are often spared and the sites of election are the extensor surfaces of the limbs, the buttocks and the chest occasionally nearly the whole body surface may eventually be affected. The primary lesions are pink to purplish erythematous,

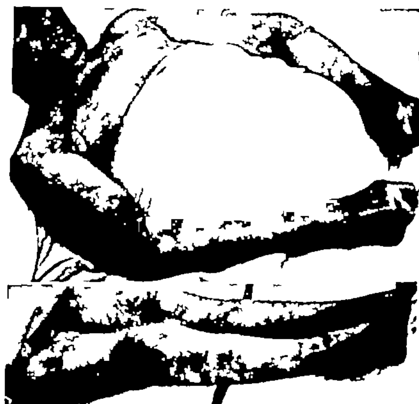


Fig 95
Acrodermatitis chronica atrophicans

slightly infiltrated patches reminiscent of erythema chronicum migrans or erysipeloid More obvious even nodular infiltration may develop in the region of the knee and elbow joints Slow extension of the lesions is accompanied by the appearance of atrophy so that the skin becomes thin and papyraceous or collodion like and loses its elasticity (Fig 95) Sweat and sebum secretion are diminished and with the disappearance of the infiltrate the veins in the diminished subcutaneous tissue

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by the age of one year The clinical picture is quite characteristic, the main features being a symmetrically-distributed rash, total alopecia and bouts of diarrhoea The rash consists of patches of moist erythematous and scaling skin with vesicles and pustules especially at the periphery sites of election are the face, particularly around the mouth and eyes, the nape of the neck, buttocks genitals, knees, elbows, hands and feet. Other lesions include paronychia and nail dystrophy blepharitis and



Fig 96

Acrodermatitis enteropathica

[*L J A Loewenthal* Heinemann]

glossitis. The child has a mournful expression is photophobic and characteristically holds his head to one side (Figs 96 and 97)

The disease is chronic and exacerbations of the superficial lesions coincide with attacks of diarrhoea Growth is retarded, the general condition is poor and the child is depressed and miserable. The mortality rate is high the child often dying of inanition or secondary infections after months or years symptoms may however persist into adult life

In a fatal case studied by Danbolt little erosions surrounded by hyperaemia were found in the large intestine microscopic examination showed granulation tissue of a non-specific, subacute character An increase of glia fibrils in the cerebral medulla and a suggestion of inhibited myelinization were also noted.

It has been suggested that acrodermatitis enteropathica may be a manifestation of moniliasis and it bears some



FIG 97
Acrodermatitis enteropathica.
[L. J A Loewenthal Heuleneri]

resemblance to kwashiorkor which is directly due to defective nutrition. Danbolt believes it to be a disease entity and considers the primary lesions to be those of the intestine

Treatment with diodoquin (210 mg 3 to 4 times daily) may have a remarkable effect on the disease, and hair growth is resumed even in cases that have long been bald. As diodoquin is not absorbed from the bowel its action must be assumed to be on the lesions of the intestinal wall no intestinal parasites have ever been found in this disease Diodoquin may have to be administered continuously or intermittently for very long periods, together with antibiotics and vitamins if necessary to

achieve cure Chloroquine is also reported to have a suppressive effect. It is not yet possible to say whether the occurrence of the disease in families means that a hereditary predisposition is involved

THE VOGT KOYANAGI SYNDROME

This is a rare disease, possibly of microbic origin, affecting tissues of ectodermal origin such as the eye, ear skin and hair The first and most constant sign is uveitis chronic, bilateral



FIG 98

Lymphostatic verrucosis

[L J A Loewenthal Annals of Tropical Medicine and Parasitology]

and extensive that may rapidly progress to blindness. Iritis, secondary glaucoma and bilateral detachment of the retina are frequently seen In 50 per cent of cases there is hyperaesthesia to sound going on to partial or complete deafness.

Cutaneous signs appear three weeks to three months after the disease begins Poliosis is common and the hair of the scalp eyelashes and eyebrows and even other hairy areas show patchy whitening this may persist or return to normal Vitiligo transitory or persistent, is a little less frequent it is symmetrical and is apt to extend Alopecia with the distribution of alopecia areata, but without the characteristic hair

stumps, is seen in 50 per cent of cases the hair generally grows again.

General signs are usually unimportant but fever and malaise occur in some cases and, much more rarely meningitic or encephalitic manifestations with inflammatory changes in the cerebro-spinal fluid.

The disease progresses towards partial or complete blindness and deafness. Cutaneous changes may return to normal No effective treatment is known.

LYMPHOSTATIC VERRUCOSIS (ROBLES AND LOEWENTHAL)

This condition is characterized by the development of a velvety texture of the skin of the feet and legs, and subsequently of a verrucous papillomatosis with fibromas and ulcerations (Fig 98) The disease appears to be endemic in certain areas of Africa and Central and South America. It seems to be the result of oedema. The same condition has been noted in amputation stumps, particularly after recurrent erysipelas has produced chronic oedema and it is probable that chronic infection is the primary factor in lymphostatic verrucosis.

Similar changes in the skin may be found in filariasis. The lesions of chromoblastomycosis (mossy foot) may closely resemble those of lymphostatic verrucosis, but the identity of the latter was established by Loewenthal

Treatment. The wearing of elastic bandages may bring some improvement, and the verrucosities may be reduced with scalpel or curette.

CHAPTER XII

TUBERCULOSIS

UNTIL 1882 when Koch discovered the tubercle bacillus (*Mycobacterium tuberculosis*) the term tuberculosis was used simply in a morphological sense to describe certain diseases characterized by histological tubercle formation Only two skin diseases, scrofula and lupus vulgaris were thus classified and some writers even excluded the latter because caseation is not an important feature The discovery of the tubercle bacillus and the recognition of the histological changes it could produce altered the whole concept of cutaneous tuberculosis and today many skin conditions of tuberculous origin are recognized It is important to recall that primary infection with tuberculosis almost always takes place in childhood and that it rarely begins in the skin Infection in childhood usually takes the form of a small caseous lesion in a lung with caseation of the regional hilar glands, the Ghon complex This process does not become chronic it either heals or spreads rapidly by continuity or by haematogenous dissemination Evidence of healed tuberculosis (immunological or otherwise) is demonstrable in most healthy adults

The first classification of skin tuberculosis, and one still used was that of Darier who spoke of *true tuberculosis* and *tuberculides* Diseases of the first group are characterized by the presence of tubercle bacilli and a typical tuberculous histological picture the group includes tuberculous ulcers and chancres, verrucous fungating vegetating and gummatous (scrofulous) tuberculosis, and lupus vulgaris

In diseases of the second group the tuberculides, the tubercle bacillus is seldom demonstrable and the histological picture is not always entirely typical of tuberculosis Their tuberculous nature is suspected for the following reasons (1) They occur in people with active tuberculosis of other organs, e g *lungs bones lymph glands or elsewhere* on the

skin. (2) They often present a histological picture suggestive of tuberculosis. (3) In rare cases the presence of tubercle bacilli can be demonstrated in the lesions by staining or culture or by animal inoculation. (4) The tuberculin reaction is positive, often strongly positive

The type of lesion produced by the tubercle bacillus depends on a number of factors (1) The mode of infection, endogenous or exogenous. (2) The allergic or immunological status of the patient with regard to tuberculosis. (3) The site in the skin where the bacillus lodges.

A tuberculous infection of the skin may be hetero- or auto-exogenous or endogenous In the hetero-exogenous group are primary inoculation tuberculosis or tuberculous chancre, verrucous tuberculosis and most cases of lupus vulgaris. Auto-exogenous infections result from contamination of the skin or mucosa by infected sputum, urine or faeces. Endogenous infections result from direct or blood or lymph spread from an infected organ to the skin.

Basic histopathology The tubercle, which is the characteristic lesion of tuberculosis in any organ, consists of a mass of epithelioid cells with some Langhans giant cells surrounded by a zone of lymphocytes. The epithelioid cells may show varying degrees of caseation. Tubercles are not always recognizable and often there is an infiltrate of epithelioid cells, with or without giant cells or necrotic changes, surrounded by lymphocytes. Such reactions occur only in patients who have developed a degree of immunity against the tubercle bacillus and they are by no means specific, for a tuberculoid reaction may develop in other microbic diseases such as leprosy and syphilis and may be seen around certain foreign bodies and in sarcoidosis.

The changes seen in primary inoculation skin tuberculosis of non-immune subjects (experimental animals tuberculous chancre) are originally entirely different. At first there is marked inflammation with many polymorphs and tubercle bacilli. After a week or two the polymorphs are gradually replaced by epithelioid cells and lymphocytes, and tubercles or tuberculoid structures appear in the skin and in the regional glands the number of bacilli declines rapidly as epithelioid lls appear

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remains an important feature. Similar changes occur in the regional glands.

Tuberculin tests are initially negative, but become positive as the disease progresses.



Fig. 99
Tuberculous chancre.
Sir John Bagshaw

TUBERCULOUS ULCERS

These lesions result from local auto-exogenous infection in patients suffering from "open" tuberculosis of some organ. The mouth and the anal and sometimes the genital regions are the usual sites of election.

In the mouth the tongue is oftenest affected, but lesions may arise on the cheeks, palate gums, fauces or lips (Fig 100) One or more lesions may be present they begin as hard papules in the mucosa, ulcerate and spread Such ulcers are commonly very tender and painful and slow to heal Regional glands may be affected Carcinoma and syphilis may be simulated



Fig 100
Tuberculous ulcers.

Anal lesions may be solitary fissured ulcers or one or more deep spreading ulcers. Anal fissures, carcinoma, syphilis and lymphogranuloma venereum have to be considered in differential diagnosis.

On the genitals there may be ulcers around the urinary meatus in both sexes or on the labia.

Caseation (necrosis) is the result of the action of products of bacterial degeneration and sometimes, in the case of haematogenous infections, of obliterative vascular changes as well. It is usually found in lesions containing many tubercle bacilli. Tuberculin skin reactions are usually weak or negative in patients with caseous tuberculosis

Tubercle *formation is associated with few bacilli and* positive or strongly positive tuberculin reactions.

Experimental studies have shown that the cellular components and architecture of tuberculous reactions are related to the various chemical constituents of the bacillus. Tuberculoprotides stimulate production of epithelioid and Langhans giant cells lipids elicit an epithelioid and giant cell reaction with caseation, glycerides produce a diffuse epithelioid-cell reaction Tuberculo-glucides cause an inflammatory reaction similar to that seen in erythema nodosum and the capsule elicits a foreign body giant cell reaction Pure caseation cannot be reproduced experimentally

The clinical varieties of cutaneous tuberculosis will be described under the broad headings of true tuberculosis and tuberculides other systems of classification will be discussed thereafter

TRUE TUBERCULOSIS

TUBERCULOUS CHANCRE

This term is reserved for the ulcerative lesion produced by primary inoculation of the tubercle bacillus into a non immune skin Children often of tuberculous parents are usually affected because most adults have developed some immunity as a result of a primary lung infection during childhood

The condition begins as a papule or nodule oftenest about the face or lips *but sometimes elsewhere that soon breaks down* and ulcerates (Fig 99) The ulcer resembles that of primary syphilis and the regional glands enlarge and may break down and form sinuses. Tuberculous penile chancre rarely results from contact with a woman with genital tuberculosis.

Histopathology In the first 2 to 3 weeks the picture is one of acute inflammation necrosis and ulceration tubercle bacilli are plentiful Later epithelioid and Langhans giant cells appear and bacilli diminish in numbers, but caseation

remains an important feature Similar changes occur in the regional glands.

Tuberculin tests are initially negative, but become positive as the disease progresses.



Fig. 99
Tuberculous chancre.
(St John Hospital)

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Fig. 101
Tuberculous gumma.
[F. W. R[illegible]]



Fig. [illegible]
Tuberculous gumm[a]
[[illegible]]

Histopathology The picture is typically tuberculous with caseation and bacilli are demonstrable

Tuberculin tests are negative or weakly positive

TUBERCULOUS GUMMA

(Scrofuloderma, tuberculosis cutis colliquativa)

In the majority of cases gummatous tuberculosis of the skin results from direct or lymphatic spread of the disease from an

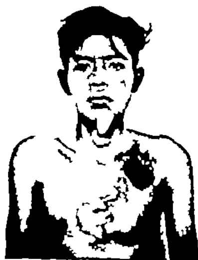


Fig. 3

Tuberculous gumma.

[*W. van der Molen*]

underlying bone or lymph gland. Gummas may also arise along the line of a lymph vessel and, exceptionally result from blood spread to the subcutaneous tissue Children are oftenest affected, with the glands and skin of the neck a common site (Figs. 101 102 and 103)

The first sign in the skin is a dark red to blue nodule or indurated hypodermal plaque This softens and discharges its ontents and an ulcer with undermined edges and a dirty necrotic base forms. An established lesion may show one or more lcers and sinuses surrounded by bluish indurated skin



FIG. 1
Tuberculous gumma.
[[illegible]]



FIG. [illegible]
Tuberculous gumma.
[[illegible]]

is often seen and pus may be expressed from cracks. One or several lesions may be present. Spontaneous healing is rare.

A similar picture may be produced by syphilis, sporotrichosis and other chronic infections it is sometimes impossible clinically to differentiate verrucous tuberculosis from chromoblastomycosis.

Histopathology The picture is, on the whole, not typically tuberculous, but tubercles are usually to be found in the dermis



FIG. 94
Verrucous tuberculosis
St John Hospital

and bacilli are present. The main features are hyperkeratosis and papillomatosis of the epidermis with a dermal infiltrate of polymorphs and lymphocytes.

The tuberculin test is weakly positive.

LUPUS VULGARIS

This is the commonest type of tuberculosis of the skin and it generally begins in childhood or adolescence as a heterogenous infection of the nasal mucosa or face. The primary lesion in all the clinical varieties is the lupoma or "apple-jelly

which often scales considerably Multiple ulcers may coalesce to form one large serpiginous lesion. Healing is slow and leaves ugly hypertrophic scars Syphilitic gumma and actinomycosis may have to be considered in differential diagnosis.

Under this heading we may mention *generalized tuberculous adenitis* which occurs in all races, but is fairly common in the South African Bantu The enlarged glands may be small and discrete or large and matted and may or may not eventually break down and affect the overlying skin It is often impossible to distinguish this condition from lymphoma on clinical grounds alone

Histopathology A typical tuberculous picture with caseation and tubercle formation is seen and tubercle bacilli are demonstrable

The tuberculin reaction is weakly positive

FUNGATING AND VEGETATING TUBERCULOSIS

The lesions of this variety are large soft moist granulomatous growths reminiscent of those seen in mycosis fungoides, fungating carcinoma or blastomycosis The mode of infection is auto- or hetero-exogenous and a site of election is the ano-genital region Elephantiasis may follow healing Fungation may of course, be a secondary phenomenon on other tuberculous lesions such as gummas

Histopathology The picture is typically tuberculous and bacilli are present

The tuberculin test is weakly positive

VERRUCOUS TUBERCULOSIS

(*Tuberculosis verrucosa cutis, verruca necrogenica*)

This form of tuberculosis results almost always from hetero-exogenous infection in an adult. It is seen on the fingers or hands of people who work with infected material e.g doctors, autopsy room attendants, butchers, etc. or it may arise in skin damaged in street accidents or after tattooing Auto-exogenous infection may also take place, and *cases in* tuberculous manual labourers who spit on their hands at work are reported

The lesions are slowly-extending verrucous hyperkeratotic plaques with an inflammatory border (Fig 104) Some crusting



FIG. 96

Lupus vulgaris treated with [illegible].

[illegible]



FIG. 97

Lupus vulgaris

[illegible]

nodule This is a tiny (pinhead) pinkish yellow maculo-papular lesion sometimes with slight scaling, whose colour is made more obvious by pressing on the skin with a glass slide (diascopy) to blanch surrounding erythema Lupomatous tissue is as soft as butter so that a toothpick pressed gently on the surface of a lesion easily penetrates it. A lupoma may enlarge slightly and become a little elevated but unless it fuses with its neighbours to make a little plaque it never exceeds 2 to 3 mm in diameter The lupoma may disappear as a result of fibrosis or it may necrose and ulcerate the end result in both cases being an atrophic scar In old lesions it is not always possible to recognize lupomas at all times.



Fig 105
Lupus vulgaris
([illegible])

Lupus vulgaris affects the region of the face in 80 per cent of cases It is very slowly progressive and in the absence of treatment usually lasts a lifetime and eventually covers large surfaces Spontaneous healing and scarring occur in places, but evolution continues elsewhere and fresh lesions may recur in scarred areas.

Lupus planus is the commonest clinical variety and begins with one or more small yellowish or violaceous patches a few millimeters in diameter which on close inspection are found to consist of groups of lupomas These patches coalesce to form a little slightly-elevated infiltrated plaque with a thin shiny erythematous surface in which lupomas can be seen on vitro-pression As time goes on the plaque extends and cicatrization begins in the centre which becomes pearly white while the edge remains red and usually a little scaly (Figs 105 to 108) Eventually large areas are involved and show active serpiginous

Papular nodular and ulcerative and pustular lesions may also arise in rare cases. Congestion of the affected skin especially of the nose, may produce chilblain-like lesions and even vascular formations that have been called *angiomatous lupus* Diffuse congestion and scaling may produce a picture similar to that of lupus erythematosus. Elephantiasic swelling or cicatricial atresia may be seen on the lips Ectropion often



Fig. 99
Lupus vulgaris

[illegible] / Pr[illegible]]

results from affection of the lower eyelid Lupus vulgaris of th limbs is usually of the plane variety but sometimes takes erucous or sclerous and papillomatous form.

Primary involvement of the nasal mucosa is common and mucous membranes are affected primarily or by spread in the majority of cases. Ulcerative and perforating lesions are seen in the nose granulating and hypertrophic vegetating lesions in th mouth. The mucous membranes of the eye middle ear nd larynx may be affected by extension.

borders and a healed or partly healed centre in which new lesions may reappear Little ulcers may form and become covered with hard adherent crusts. The picture is reminiscent of that of a superficial syphilitic gummatous lesion, but an important diagnostic point is that a syphilitic lesion will often spread as far in a month as lupus vulgaris will in a year



Fig. 108
Lupus vulgaris.
[St Thomas' Hospital]

The other clinical types are variants of this basic form

Ulcerating and vegetating lupus often attacks the nose spreads quicker than usual and may destroy a great area of skin mucous membrane and deeper tissues

Lupus tumidus shows salient nodules and deeply infiltrated plaques covered by a thin shiny epithelium that does not ulcerate (Figs. 109 and 110) A sub-variety *myxomatous lupus* consists of yellow gelatinous masses under a tense epidermis the earlobe is often affected and may be trebled in size

Papular nodular and ulcerative and pustular lesions may also arise in rare cases. Congestion of the affected skin, especially of the nose, may produce chilblain-like lesions and even vascular formations that have been called *angiomatous lupus* Diffuse congestion and scaling may produce a picture similar to that of lupus erythematosus. Elephantiasic swelling or cicatricial atresia may be seen on the lips Ectropion often



Fig. 99

Lupus vulgaris

[illegible] *of* [illegible] (left.)

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borders and a healed or partly healed centre in which new lesions may reappear. Little ulcers may form and become covered with hard adherent crusts. The picture is reminiscent of that of a superficial syphilitic gummatous lesion, but an important diagnostic point is that a syphilitic lesion will often *spread as far in a month as lupus vulgaris will in a year*.



Fig. 108
Lupus vulgaris.
[*St Thomas' Hospital*]

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measles. It is relatively benign and usually heals in a few months, but the occasional development of a true chronic lupus shows that it should be classified with lupus vulgaris rather than with the benign tuberculides or disseminated miliary tuberculosis which is usually fatal.



Fig.
Squamous-cell carcinoma on lupus vulgaris.
(St Thomas' Hospital)

Histopathology Tubercules and plaque-like infiltrates of epithelioid cells surrounded by lymphocytes are seen in the dermis and may extend deeply to the hypoderm in places. Caseation is not a marked feature and may be absent. The epidermis may be atrophic as a result of pressure of infiltrate or even ulcerated away. It may show hyperkeratosis and papillomatosis. Tubercle bacilli are rarely seen in sections, but their presence may be demonstrated by animal inoculation.

Tuberculin tests are positive

Secondary infections such as impetigo and even erysipelas may complicate the picture and recurrent erysipelas may lead to elephantiasis. Squamous carcinoma is a grave complication



FIG. 110
Lupus vulgaris
[Leeds]

that supervenes on old lupus lesions the use of radiotherapy increases this risk (Fig 111)

Tertiary syphilis, leprosy sarcoidosis, lupus erythematosus, leishmaniasis blastomycosis and occasionally psoriasis may be simulated

Disseminated eruptive lupus vulgaris is a distinct entity which results from haematogenous spread of tubercle bacilli and consists of suddenly-developing plaques of lupomatous lesions (rarely verrucous lesions) particularly on the trunk. The eruption occurs in children, especially after a fever such as

and limbs (Figs. 112 and 113) Annular patterns may be produced by central healing in a plaque, and irregular or polycyclic patterns by confluence. The lesions are rarely moist but may sometimes look eczematous. Lichen scrofulosorum is usually seen in children or adolescents with glandular osseous or pulmonary



Fig.
Lichen scrofulosorum.
[University of

tuberculosis, and its appearance may be precipitated by an intercurrent infectious fever The eruption may heal after a few months or disappear and reappear over months or years.

Similar eruptions are seen in other infective diseases such as chronic coccal or fungous infections and in secondary syphilis lichen planus, keratosis pilaris and pityriasis rubra pilaris.

Histopathology Typical tuberculoid structures with lymphocytes surrounding epithelioid and giant cells are seen particularly around hair follicles, but also apart from them in the dermis. A spotty infiltration of the stratum Malpighii with lymphocytes may be seen, and this is considered by

MILIARY TUBERCULOSIS

Skin lesions are sometimes seen in miliary tuberculosis together with lesions in other organs (meninges, etc.) as a result of haematogenous spread of bacilli in an anergic patient The eruption is generalized appears suddenly, and consists of small brownish red papules or papulo-vesicles that may necrose and form ulcers. Miliary tuberculosis is generally *rapidly fatal*

Histopathology There is an acute inflammatory reaction in the dermis with oedema, polymorphonuclear leukocytic infiltrate and necrosis but only rarely is there time for any tuberculoid picture to develop Tubercle bacilli are numerous.

Tuberculin tests are negative

THE TUBERCULIDES

The tuberculides are bacterial allergides and result from haematogenous dissemination of tubercle bacilli from some active chronic focus of infection (in an organ or even in the skin itself) *in a person who has developed a high degree of immunity* As in all such reactions, it is rare to discover the causative organism in the lesions because the whole purpose of the reaction is destruction of the allergen It is not always immediately possible to find the primary focus of infection and the diagnosis may rest only on strongly positive tuberculin tests and a tuberculoid histological structure The appearance of tuberculides *is not necessarily of grave significance as they occur* only in immune subjects A given patient may develop different varieties of tuberculides in one or in different attacks and transition forms may be noted The variety of tuberculide is determined by the type of blood vessel in which the tubercle bacillus lodges

LICHEN SCROFULOSORUM

This tuberculide is characterized by small follicular sometimes squamous lichenoid papules that are generally grouped in oval or circular plaques 1 to 5 cm in diameter on the trunk

and limbs (Figs. 112 and 113) Annular patterns may be produced by central healing in a plaque, and irregular or polycyclic patterns by confluence. The lesions are rarely moist but may sometimes look eczematous. Lichen scrofulosorum is usually seen in children or adolescents with glandular osseous or pulmonary



FIG.
Lichen scrofulosorum.
(Courtesy of Pr...)

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Civatte to be a feature of the tuberculides Tubercle bacilli are rarely demonstrable in sections or by animal inoculation.

The tuberculin test is strongly positive



FIG. 1 3
Lichen scrofulosorum.
[St John's Hospital]

PAPULO-NECROTIC TUBERCULIDES

Disseminated papular papulo-pustular and papulo-necrotic lesions of the face or of the limbs hands and feet and, rarely the trunk are seen in adolescents and young adults with chronic tuberculosis This form is arbitrarily divided into *acnitis* when the face is particularly affected and *folliclis* when the limbs are affected The lesions are deep hard, bluish red papules or little nodules that usually evolve towards scaling

crusting, suppuration, necrosis and ulceration (Figs 114, 115 and 116) Healing takes place in a few months leaving pigmentation and scars, but fresh lesions appear in crops over months or years.

The allergic vascular reaction which takes place may at times be brusque and severe so that purpuric, necrotic and vesicular papules may be seen, especially on the limbs this variety is known as black or purpuric tuberculide (Gougerot)



FIG. 4
Papulo-necrotic tuberculide.
(St Thomas' Hospital)

Acne vulgaris, acne necrotica, dermatitis nodularis necrotica, follicular coccal infections and pustular secondary syphilides have to be considered in differential diagnosis. Papulo-necrotic ide eruptions may be caused by organisms other than the tubercle bacillus.

Histopathology A small area of necrosis involving the superficial dermis and overlying epidermis is surrounded by a zone of non-specific inflammation in which some tubercles can be recognized. The arterioles and venules of the deeper dermis show endarteritis and endophlebitis with thrombosis and these changes account for the central necrosis. Tubercle bacilli are not usually demonstrable.

Tuberculin tests are strongly positive

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The tuberculin test is strongly positive.



FIG. 115

Lichen scrofulosorum.

[St John Hospital]

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SMALL PAPULAR AND MILIARY TUBERCULIDES

The rare small papular or miliary tuberculides differ from the papulo-necrotic tuberculides not only in size but in their evolution, which is usually towards healing without suppuration or ulceration. The face and neck are usually affected,



Fig. 7

Small papular tuberculide with tuberculous adenitis.

rarely the trunk and limbs. The lesions are numerous, pin head size or a little larger yellowish to red in colour and sometimes slightly scaling or crusted. They show a yellowish lupoid colour on vitropression. The lesions appear in crops over months or years and healing may leave small scars or yellowish-brown pigmentation (Fig 117)

FIG. 1 5

Papulo-necrotic t berculide with t berculous gumma. Positive t berculin test.



FIG 6

Papulo-necrotic t berculid

Small papular and miliary tuberculides

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Sarcoidosis, early lupus vulgaris, acne vulgaris and rosacea may all have to be considered in differential diagnosis and convincing evidence of the existence of tuberculosis elsewhere is essential before this type of tuberculosis is diagnosed. Rosacea may give just such a clinical and histological picture and the phenomenon has been called the rosacea like tuberculide of Lewandowsky there are few, however who still accept this as a tuberculide

Histopathology Tubercles or epithelioid-cell infiltrates with varying degrees of lymphocytic infiltration and central necrosis may be seen Differentiation from sarcoidosis on the one hand and lupus vulgaris on the other may be impossible on histological grounds alone

Tuberculin tests are strongly positive

Ulcerative tuberculides

These are the rarest of the tuberculides and consist of one or more torpid painless ulcers with an irregular undermined edge, grey and necrotic or granulating floor and slightly indurated base Any area may be affected but there is a predilection for the legs where the lesions may resemble varicose ulcers.

The histological picture may include tuberculoid structures, but is seldom typical of tuberculosis and the diagnosis is usually made by inference because other types of tuberculides are also present and tuberculous lesions are discovered elsewhere.

Erythema induratum (Bazin)

Erythema induratum Bazin's disease is a common tuberculide that occurs oftenest in girls and young women and affects the backs and sides of the lower halves of the legs and very rarely other areas of skin (Figs. 118 and 119) The lesions are painful hypodermal nodules or nodular infiltrates over which the skin is bluish or violaceous, tense and often scaly Some nodules may soften and ulcerate deeply or discharge through fistulae producing a picture reminiscent of tuberculous gumma Healing whether there is ulceration or not is followed by slightly depressed and often pigmented scars The disease often recurs, usually each winter and an established case will show

Fig. 8
Erythema Induratum
[L. J. A. [illegible]]



Fig. 9
Erythema induratum.
[Sir John [illegible]]

old scars as well as fresh nodules and possibly ulcers. Erythrocyanosis and oedema of the ankles and chilblains are often associated and other tuberculides (papulo-necrotic) may occur elsewhere at the same time

Tuberculous erythema nodosum may sometimes run a sub-acute course with lesions closely resembling those of erythema induratum and transition forms link the two conditions

Hypodermal streptococcides, identical clinically and histologically with erythema induratum are sometimes encountered in which the diagnosis is usually determined by a process of exclusion since the identification of the causative streptococci involves techniques of asepsis difficult to attain in ordinary practice.

The distribution of lesions in erythema induratum is usually sufficient to distinguish it from sarcoidosis with hypodermal nodules, but the histological pictures may be similar The condition known as *disseminated nodular sarcoids of Darier* with lesions on the extensor surfaces of the limbs and occasionally on the trunk and face may be considered as a variant of erythema induratum Syphilitic gummatous nodules and ulcers may occur on the legs, but patients are usually adults over thirty and a serum test will establish the diagnosis

Histopathology There is a largely non specific lymphohistiocytic and plasma cell infiltrate in the hypoderm and deeper part of the dermis with areas of tuberculoid structure and, sometimes tubercles Both types of infiltrate penetrate between the fat cells and gradually replace them (proliferation atrophy or *wucheratrophie*) Varying amounts of caseation are seen. The primary change is one of proliferative vasculitis of all sizes of vessels but especially the large arteries and veins Their walls are infiltrated with round cells and become thickened thrombosis and obliteration result and lead to necrosis and abscess formation Tubercle bacilli are rarely demonstrable and this, with the vascular changes, helps to distinguish erythema induratum from tuberculous gumma the presence of necrosis and the vascular changes will usually distinguish it from acute erythema nodosum and hypodermal sarcoidosis.

Tuberculin tests are strongly positive

ERYTHEMA NODOSUM

Some, but not the majority of, cases of erythema nodosum are tuberculides. Young subjects are affected and they are usually suffering from a primary tuberculous infection. The lesions are firm, red to violaceous, tender dermo-hypodermal swellings that appear in crops on the anterior surfaces of the legs and sometimes on the thighs and arms. As they heal colour changes like those seen in a bruise take place until the skin becomes normal again. The life of a lesion is 10 to 20 days and an attack lasts several weeks. There may be only a few or several dozen lesions. Tuberculous erythema nodosum seldom recurs. The tuberculin test may increase in positivity during the period of observation Evolution to erythema induratum has rarely been noted Tubercle bacilli have occasionally been demonstrated in the lesions. Erythema nodosum is fully considered in Chapter VII

CLASSIFICATION

The lesions just described are today recognized as manifestations of tuberculosis. For Darier the concept was even broader he included the sarcoids of Besnier Boeck-Schaumann and of Darier Roussy lupus erythematosus, granuloma annulare and lichen nitidus, some of which may show a tuberculoid histological picture

It is known today that a tuberculoid reaction may be produced by other chronic bacterial infections or even by non-bacterial causes and it is seen, e g in syphilis, leprosy and leishmaniasis and as a foreign body reaction in acne conglobata and beryllium granuloma. It can be reproduced artificially in the tuberculin reaction a weak positive reaction shows only a banal inflammatory infiltrate, but a strong positive (in a person with well-developed immunity) shows a tuberculoid tissue change Inoculation of tissue from a positive test site naturally does not reproduce the disease as it is caused by the chemical constituents of the bacilli whether living or dead

Lesions clinically and sometimes histologically typical of tuberculosis are produced by other causes erythema induratum

old scars as well as fresh nodules and possibly ulcers. Erythrocyanosis and oedema of the ankles and chilblains are often associated and other tuberculides (papulo-necrotic) may occur elsewhere at the same time

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Tuberculin tests are strongly positive

but there are few or none to be seen in an old case which may be considered almost as a tuberculide.

Here is a plan of classification on this basis (after Lutz)

Mode of Inoculation	*Allergic Status of Patient*		
	Anergic	*Medium*	*Hypergic*
Solitary site usually exogenous.	Tuberculous chancre. Tuberculous ulcer in cachectic patient.	Lupus vulgaris. Verrucous tuberculosis. Tuberculous gumma.	Experimental animals only
Multiple sites, usually haematogenous	Miliary tuberculosis.	Disseminated lupus vulgaris.	The tuberculides.

The site where circulating tubercle bacilli lodge and the vessels involved have a bearing on the type of lesion produced. When the bacilli lodge in small dermal vessels papular and papulo-necrotic lesions result, but when they lodge in large deep hypodermal vessels nodular lesions are produced, and caseation as a result of vascular occlusion occurs quite apart from that produced by direct bacillary action. Classifications based on histological changes or on the mode of infection (primary or secondary) can be superimposed on the basic plan according to the allergic state of the patient.

TREATMENT

The prognosis in cutaneous tuberculosis has been vastly improved in recent years by the use of the potent modern anti-tuberculous remedies, in particular streptomycin and isoniazid. In other days most cases of lupus vulgaris were doomed to be treated to the end of their days today cure is confidently to be expected.

LUPUS VULGARIS

Calciferol vitamin D2 deserves to be mentioned first although it is no longer commonly used except in cases resisting other types of treatment. The discovery by Charpy in the

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Lupus erythematosus and granuloma annulare, both probably allergic diseases may well sometimes be due to tuberculosis but few people today would call them tuberculides evidence for such a classification is almost invariably dubious or wanting Lichen nitidus is considered to be only a variety of lichen planus Sarcoidosis is thought by some to be an epithelioid cell reticulosis unrelated to tuberculosis, and others consider it an individual type of reaction to a variety of stimuli of which the tubercle bacillus is only one

In the past many theories were advanced to explain the difference between true (bacilli-containing) tuberculous lesions and the tuberculides It was suggested that tuberculides were caused by a tuberculous toxin (but the tubercle bacillus makes no exotoxin) an attenuated tubercle bacillus a tuberculous virus or by some different organism through the mechanism of biotropism

There now seems no doubt that all the manifestations of tuberculosis in the skin are caused by the tubercle bacillus itself and that the type of reaction depends mainly on the allergic (or immunological) status of the patient with regard to the infecting organism If the patient has no acquired immunity one sees lesions of true tuberculosis with many bacilli if he has developed a high degree of immunity as a result of chronic infection we see the tuberculides in which the causative bacilli have been destroyed and only characteristic histological changes suggest that they once were present

The development of immunity against the tubercle bacillus is often a rapid process and may be sufficient to cause spontaneous cure in cases of primary or re infection tuberculosis of any organ Spontaneous cure is to be expected in the case of the tuberculides A degree of immunity insufficient to destroy all the organisms is found in lupus vulgaris. Lupus vulgaris is usually a hetero-exogenous infection in a patient who has recovered from a primary infection and thus has some immunity bacilli can often be demonstrated in early lesions,

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The site where circulating tubercle bacilli lodge and the vessels involved have a bearing on the type of lesion produced. When the bacilli lodge in small dermal vessels papular and papulo-necrotic lesions result, but when they lodge in large deep hypodermal vessels nodular lesions are produced, and caseation as a result of vascular occlusion occurs quite apart from that produced by direct bacillary action. Classifications based on histological changes or on the mode of infection (primary or secondary) can be superimposed on the basic plan according to the allergic state of the patient.

TREATMENT

The prognosis in cutaneous tuberculosis has been vastly improved in recent years by the use of the potent modern anti tuberculous remedies, in particular streptomycin and isoniazid In other days most cases of lupus vulgaris were doomed to be treated to the end of their days today cure is confidently to be expected.

Lupus vulgaris

Calciferol, vitamin D_2 deserves to be mentioned first although it is no longer commonly used except in cases resisting other types of treatment. The discovery by Charpy in the

may also be caused by streptococci erythema nodosum by streptococci or by drug sensitivity papulo-neurotic lesions by a variety of organisms and lichen scrofulosorum by coccal or fungous infections.

Lupus erythematosus and granuloma annulare both probably allergic diseases, may well sometimes be due to tuberculosis but few people today would call them tuberculides evidence for such a classification is almost invariably dubious or wanting Lichen nitidus is considered to be only a variety of lichen planus Sarcoidosis is thought by some to be an epithelioid cell reticulosis unrelated to tuberculosis, and others consider it an individual type of reaction to a variety of stimuli of which the tubercle bacillus is only one.

In the past many theories were advanced to explain the difference between true (bacilli-containing) tuberculous lesions and the tuberculides It was suggested that tuberculides were caused by a tuberculous toxin (but the tubercle bacillus makes no exotoxin) an attenuated tubercle bacillus, a tuberculous virus or by some different organism through the mechanism of biotropism

There now seems no doubt that all the manifestations of tuberculosis in the skin are caused by the tubercle bacillus itself and that the type of reaction depends mainly on the allergic (or immunological) status of the patient with regard to the infecting organism. If the patient has no acquired immunity one sees lesions of true tuberculosis with many bacilli if he has developed a high degree of immunity as a result of chronic infection we see the tuberculides in which the causative bacilli have been destroyed and only characteristic histological changes suggest that they once were present.

The development of immunity against the tubercle bacillus is often a rapid process and may be sufficient to cause spontaneous cure in cases of primary or re-infection tuberculosis of any organ Spontaneous cure is to be expected in the case of the tuberculides A degree of immunity insufficient to destroy all the organisms is found in lupus vulgaris Lupus vulgaris is usually a hetero-exogenous infection in a patient who has recovered from a primary infection and thus has some immunity bacilli can often be demonstrated in early lesions,

but there are few or none to be seen in an old case which may be considered almost as a tuberculide.

Here is a plan of classification on this basis (after Lutz)

Mode of Inoculation	*Allergic State of Patient*		
	Anergic	*Allergic*	*Hyperergic*
Solitary site, usually cutaneous	Tuberculous chancre. Tuberculous ulcer in cachectic patient.	Lupus vulgaris. Verrucous tuberculosis. Tuberculous gumma.	Experimental animals only
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Lupus vulgaris

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early 1940 s, that calciferol in high dosage could cure lupus vulgaris was the first major advance in the treatment of the disease. Cod liver oil had been used with some success a century before by Emery who gave massive doses of 700 to 1 000 g daily but smaller doses used subsequently by other workers were ineffective and the method for obvious reasons, was abandoned

Calciferol available in tablet form or in alcoholic solution, is given in doses of 50 000 units thrice daily for the first month and then 50 000 units twice daily for at least six months or until the disease is cured Treatment is usually well tolerated, but it must be suspended if anorexia loss of weight digestive upsets, polydypsia or polyuria develop Toxic effects are related to increased serum calcium levels and renal damage a routine check on the urine blood urea and serum calcium should be made at least once a month

Calciferol appears to act by increasing tissue resistance to the tubercle bacillus and it is probable that the Finsen treatment commonly used in other days acted by increasing the vitamin D content of the skin

Isoniazid (isonicotinic acid hydrazide) is the remedy most popular at present Dosage is in the range of 3 to 6 mg per kilo body weight per day and the average dosage for adults is 100 mg thrice daily Minor toxic effects such as digestive upsets and dizziness are fairly common but seldom sufficient to cause suspension of treatment Treatment must continue until all lesions are apparently cured Patients should of course be kept under observation long after clinical cure as relapse may occur and require resumption of treatment

Streptomycin alone is not advocated in lupus vulgaris, but it may at times be used to advantage with isoniazid or calciferol A dose of 1 g is given three times weekly

Para aminosalicylic acid may be used in conjunction with isoniazid or streptomycin alone it is ineffective It is little used for purely cutaneous tuberculosis

Surgical excision is the method of choice when the lesion is small and accessible Some writers still recommend the use of Finsen therapy destructive pastes scarification, etc., as well as chemotherapy but these are rarely necessary X ray therapy must not be used for lupus vulgaris.

VERRUCOUS TUBERCULOSIS

This seldom responds rapidly or satisfactorily to chemotherapy and excision or diathermy destruction are frequently necessary

TUBERCULOUS GUMMAS

Gummas are usually responsive to isoniazid and streptomycin, but are unaffected by calciferol. Excision of discrete lesions is advisable when it is feasible. Cure is hastened and the cosmetic result is good.

In other varieties of true tuberculosis and in most cases of tuberculides the treatment of the primary focus is all-important and that of the skin lesions is only symptomatic. Degos claims good results in cases of papulo-necrotic tuberculide treated with vitamin C in daily doses of 1·5 g intravenously for a month. The use of occlusive, supportive bandages (e.g. Viscopaste) is of value in erythema induratum.

Preliminary reports on cycloserine, an antibiotic obtained from various streptomyces species, suggest that it may be effective against tuberculides but not lupus vulgaris. A total dose of 0·75 to 1 g daily is used

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CHAPTER XIII

LEPROSY

LEPROSY is a specific infective disease caused by the acid fast *Mycobacterium leprae* (Hansen's bacillus) The disease is now encountered in endemic form mainly in the tropical belt, but it was in the past, common in Europe. It has virtually disappeared from Europe as a result of rising standards of hygiene and the application of strict rules of segregation About 50 per cent of cases of leprosy are contracted before puberty and in children the incidence in the sexes is roughly the same. Adult men are infected much oftener than women perhaps because the men in endemic areas have much greater opportunities for contact with infected people than have the women who are more confined in their movements. It is estimated that there are probably between 2 and 4 million lepers in the world today

Skin and nerve lesions are the most important in leprosy but *M leprae* has been demonstrated at times in every organ The bacillus is demonstrable by direct microscopy in the skin and nerves with ease in lepromatous leprosy but in only about 20 per cent of cases of tuberculoid and indeterminate leprosy It has not so far been cultured and lesions comparable to those in man are not seen in experimental animals

Infection with leprosy probably results from contact with an infected person or with excretions such as sputum and nasal mucus which may contain large numbers of bacilli The site of primary infection is the skin in most cases and entry of the bacillus through mucous surfaces is believed to be rare Spread of infection by insect vectors is theoretically possible but there is no practical proof that this does occur Mediate infection *via* clothing or bedding is unlikely

The incubation period of leprosy is not accurately known, but it is generally measured in years in rare cases it seems to have been much shorter as for example when an infant aged forty-eight days showed evidence of infection

The primary lesion on the skin is almost always solitary and generally on exposed skin. In young South African negroes it is commonly situated on the thighs or buttocks suggesting that contact with sputum or nasal discharges is involved. This lesion is in the form of a small patch of skin showing depigmentation, erythema, hyperpigmentation or lichenoid change of these the first is most commonly seen. There is often some minor sensory disturbance in the affected area and in rare cases localized sensory disturbance alone may be noted. The primary lesion often goes unnoticed by the patient and the disease is recognized only when extension or spread occurs spontaneous cure may well sometimes take place in the early stage. Histological changes are generally non-specific and bacilli few or absent.

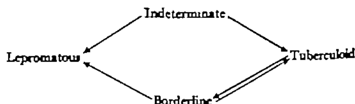
After months or years the primary lesion begins to show signs of activity the area becomes elevated and paraesthesiae may be followed by diminution or loss of sensation. Spread of the infection *via* the lymphatics, nerves, and eventually the blood stream follows, and the disease develops, in most cases, towards one or other of the polar types (tuberculoid or lepromatous) The polar types vary in relative frequency in different parts of the world in the Philippines lepromatous cases account for about 40 per cent of the total, in India for only about 20 per cent.

The manner in which the disease develops depends on the reaction of the host. If he develops resistance to the infecting organisms he will have lesions of a benign type (indeterminate or tuberculoid) if he becomes anergic the lesions will be of the malignant (lepromatous) type. The state of resistance of the patient may be determined by the use of the *lepromin test* in which 0 1 c.c. of a suspension of heat killed lepra bacilli is injected intradermally into the anterior surface of the forearm. The lepromin is prepared from lepromatous tissue taken from untreated lepers. In resistant cases an early (Fernandez) and a late (Mitsuda) positive reaction may appear *The Fernandez reaction* is a fleeting congestion and erythema with no characteristic histological changes that appears in 24 to 48 hours and fades in a few days. *The Mitsuda reaction* develops slowly thereafter as a little patch of pink to violaceous colour infiltrated and becoming nodular as it reaches its acme after

3 to 4 weeks this type of lesion has a structure typical of tuberculoid leprosy The nodule may ulcerate and it disappears slowly over some months Only the Mitsuda reaction is significant It is positive in about 90 per cent of cases of tuberculoid and indeterminate leprosy and usually negative in lepromatous leprosy Although the exact nature of the reaction taking place is not certainly known (tissue as well as bacilli is injected) its use may be of great value in diagnosis and prognosis

Leprosy begins in a benign form, probably of the indeterminate type and if the patient becomes resistant, develops later into the tuberculoid polar type or rarely remains *indeterminate If no resistance develops, change to the more* stable polar type, lepromatous leprosy takes place the Mitsuda reaction, which may at first have been positive, now becomes negative

Lepromatous leprosy once established, does not change into any other type Tuberculoid leprosy is less stable it may change, *via* borderline leprosy or directly into the lepromatous type. Borderline leprosy is an unstable phase, following usually on tuberculoid leprosy which may progress into lepromatous or regress again to tuberculoid leprosy Indeterminate leprosy is also unstable though cases may always remain at this stage The possibilities may thus be summarized



When dissemination of the disease *via* nerves lymphatics or blood takes place Hansen s bacillus shows a predilection for the skin peripheral nerves and the nasal buccopharyngeal and laryngeal mucosae Of the internal organs the liver spleen, suprarenal glands, testes and bone marrow are oftenest affected The course of leprosy is almost invariably chronic with bursts of activity alternating with periods of inactivity or even regression that may last months or years The leper usually dies of some intercurrent disease

Note Readers straying further into the literature on leprosy will discover that many leprologists use a strange and confusing language The favourite term is the macule which may be the little discoloured spot of the Latinist and of the dermatologist, but is oftener any lesion, of any size, shape or consistency of tuberculoid leprosy

TUBERCULOID LEPROSY

Tuberculoid leprosy is arbitrarily divided into minor and major forms

The lesions of minor tuberculoid leprosy are slightly elevated plaques with an irregular surface as a result of their origin from

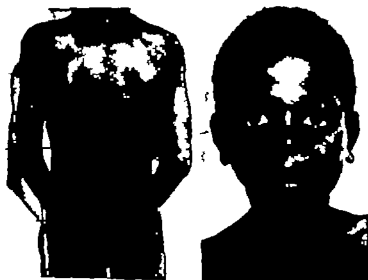


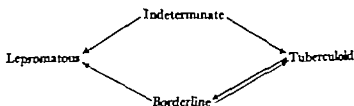
Fig 190
Minor tuberculoid leprosy
(University of Cape Town)

fairly superficial micropapular infiltrates (Fig 190) They are pink to violaceous in colour extend peripherally often coalesce and tend to central healing. In older lesions the central area is flattened and desquamating depigmentation follows, but pigment may eventually be restored. The edges remain active and elevated, but may become fragmented Sometimes

3 to 4 weeks this type of lesion has a structure typical of tuberculoid leprosy The nodule may ulcerate and it disappears slowly over some months Only the Mitsuda reaction is significant It is positive in about 90 per cent of cases of tuberculoid and indeterminate leprosy and usually negative in lepromatous leprosy Although the exact nature of the reaction taking place is not certainly known (tissue as well as bacilli is injected) its use may be of great value in diagnosis and prognosis

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eventually appear in asymmetrical pattern and nerves are involved. The scalp, palms and soles are usually spared. Some patients may continue in this state for a lifetime, the



FIG.
Top: Major tuberculoid leprosy
Bottom. Minor tuberculoid leprosy
[*R. Davson*]

lesions tending to regress and even to be entirely effaced after depigmentation and repigmentation.

In patients with less resistance this stage is followed by one of haematogenous dissemination of lepra bacilli and the appearance of symmetrically-distributed lesions. Polyneuritic symptoms rapidly increase and abscesses may form in nerve trunks

the plaques remain infiltrated Individual papular lesions also occur The intervening skin is normal.

Sensory changes are usually demonstrable in the lesions, especially in the central area, by pinprick or cotton wool test but the corresponding cutaneous nerves show no major hypertrophic changes It may be difficult in early cases to demonstrate the presence of bacilli by simple methods, but histological examination usually shows typical changes

The lesions of major tuberculoid leprosy arise from a deeper reaching infiltrate in the dermis and even the hypoderm. They are more elevated than those of the minor form and the plaques show little tendency to central healing and do not spread so far or so rapidly (Fig 121) Papular and nodular lesions also occur Superficial nerve trunks are often considerably thickened and sensory changes are often demonstrable in the skin lesions. Bacilli may be demonstrable by simple methods especially in *cases in reaction so that confusion may sometimes arise* with lepromatous leprosy In tuberculoid leprosy however lesions are often asymmetrically distributed the intervening skin is normal and the Mitsuda reaction is generally positive.

Lesions of the minor and the major types may coexist in one patient. Tuberculoid skin lesions are often termed *leprides*.

Infection of nerve trunks is commonly associated with skin lesions in tuberculoid leprosy and causes symptoms apart from the sensory changes in these lesions themselves Nerve trunks become enlarged and often beaded and sensory and other changes are first noted in the extremities. Trophic changes which may occur include anhidrosis, glossy skin, ichthyotic scaling pigmentary changes pemphigoid bullae, superficial and perforating ulcers, atrophy and necrosis of bones with subsequent mutilation and articular lesions Motor lesions with muscular atrophy and paralysis may be seen Occasionally a pure tuberculoid leprosy of nerves without skin lesions may occur and is recognized by sensory changes or patchy anhidrosis and nerve thickening

The histological changes in the skin and nerves are similar but necrosis may occur in nerves and never in skin. The evolution of untreated tuberculoid leprosy is extremely chronic. The first lesion which probably evolved from an indeterminate lesion may long be unique but leprides

A state of reaction may occur in cases of major tuberculoid leprosy and is characterized by the sudden appearance of fever exacerbation of existing lesions and the appearance of many new macules, papules and nodules of an angry reddish-violet colour that tend to ulcerate. Superficial nerve trunks swell and often become very painful. Oedema of the face, hands and feet is common. Rarely there is seen an ulcero-bullous eruption known as lazarine tuberculoid leprosy The acute phase of reaction lasts about a fortnight and then subsides. Reactions may be provoked by treatment and probably result from a dissemination of toxic products of disintegration of lepra bacilli they cannot, however always be interpreted as indicating an improvement in prognosis.

The prognosis of tuberculoid leprosy which is a relatively stable type, is good especially in cases with minimal nerve involvement and there is a certain tendency to spontaneous regression. Most tuberculoid lepers remain so for life, though they may show periods of activity and regression. Except during phases of "reaction" the lepromin test is usually strongly positive Some cases evolve to borderline leprosy a state intermediate between major tuberculoid and lepromatous, and then either regress or go over into frank lepromatous leprosy Rare cases change directly to the lepromatous

Borderline leprosy

This is a distinct phase not to be confused either with major tuberculoid leprosy in reaction or lepromatous leprosy It is, however very difficult to distinguish at first sight from tuberculoid leprosy The lesions are often asymmetrically distributed plaques with a succulent appearance and soft feel. The borders are well-defined and the colour deep red Nasal swabs are positive in about a third of cases the Mitsuda reaction is negative or feebly positive Lepra bacilli are usually demonstrable in skin lesions which show changes suggestive of both tuberculoid and lepromatous leprosy The borderline phase is extremely unstable.

Indeterminate leprosy

Most cases of leprosy probably begin in the indeterminate phase although progression to one of the polar types may have

and lead eventually to calcification. Sclerosis of connective tissue causes compression and degeneration of nerve fibres. In the upper limbs the ulnar nerve is oftenest affected. There may first be hyperaesthesia and neuralgia but often the patient only notices sensory loss. Later there is atrophy of the interosseous muscles and those of the thenar and hypothenar eminences leading to claw hand (Fig. 122). In the lower limbs

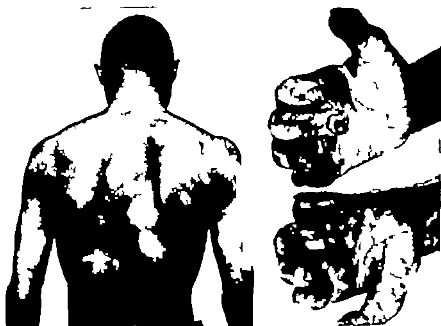


FIG. 122

Tuberculoid leprosy with claw hands.

the external popliteal, posterior tibial and sciatic nerves may suffer and lead, apart from sensory disturbances, to paresis or paralysis of the antero-external muscles of the leg and equinovarus deformity of the foot. The superficial cervical nerves are often palpably or visibly enlarged and unilateral or bilateral facial palsy may be seen particularly with states of "reaction." The trophic lesions which may develop have already been mentioned.

Mucosal lesions are rare: the nasal mucosa is affected in about 10 per cent of cases, other mucous surfaces exceptionally. Ectropion may result from periocular lesions. The eyebrows may fall if a lesion develops in that region.

plaques and diffuse infiltrated areas may be seen their colour varies from pink to reddish-blue on white skin (Figs. 123 and 124)

Lepromatous leprosy may arise from indeterminate leprosy or from tuberculoid leprosy directly or more commonly after a borderline phase. Cutaneous lesions arise in old benign lesions or on normal skin and are often symmetrically distributed on the face, neck, body buttocks and antero-external surfaces of the limbs. The first crop is usually one of papules, later appear nodules and infiltrates and finally in feeble and cachectic patients, furunculoid and ulcerative lesions.





Fig. 125
Lepromatous leprosy
[A. R. Dawson]

The mucous membranes are early involved and those of the nose, bucco-pharynx, larynx and bronchi are liable to be affected. Aphonia, dyspnoea, laryngeal stenosis and, in advanced cases, septal perforation and saddle-nose may result. The ocular conjunctiva and sclera are often attacked and recurrent, painful attacks of irido-cyclitis may lead to progressive loss of vision. The eyebrows and eyelashes frequently fall and more rarely ectropion and lagophthalmos are seen.

Epididymo-orchitis is common and is accompanied in most cases by gynaecomastia the ovaries are seldom attacked. In rare cases other endocrine glands may be affected.

Although nerve trunks are rapidly invaded polyneuritic changes are often, at first, not very marked, but symptoms

taken place before a diagnosis is made. Indeterminate leprosy *is unstable and its lesions resemble those of tuberculoid rather* than lepromatous leprosy Evolution to tuberculoid or lepromatous leprosy usually takes place and seldom does the disease stay for long in this phase it may however remain unchanged throughout life, running a relatively benign course and causing little trouble save when, rarely mutilations occur Under treatment with DDS progress is invariably towards tuberculoid leprosy

The skin lesions are generally flat, hypopigmented or erythematous plaques or macules. Hyperpigmentation is rare. Occasionally there may be a little discrete elevation of the edges of erythematous lesions. Plaques may coalesce to produce polycyclic figures Motor and sensory changes identical with those described in tuberculoid leprosy may occur but the nerves, although they may show regular hypertrophy are seldom so markedly affected

The Mitsuda reaction is usually only feebly positive but *becomes stronger if the case progresses towards the tuberculoid* negative if towards the lepromatous Bacilli are demonstrated with difficulty in the skin lesions, particularly those of the hypopigmented type Histological examination shows a banal histio-lymphocytic perivascular infiltrate except when evolution towards one or other polar type is in progress when more suggestive patterns may be seen

Evolution in the rare persistent case is more torpid than in tuberculoid leprosy and proceeds with phases of activity and regression Mucosal lesions are very rare.

LEPROMATOUS LEPROSY

This is the most stable and severe form of the disease. The bacilli are disseminated in bursts of metastasis and develop in great numbers in affected organs. At such times there are general symptoms including fever headache, somnolence and the appearance of fresh lesions in the skin mucosae nerves and other organs.

The skin lesions known as *lepromas* vary in size from small, almost imperceptible infiltrates to large tumour masses. They are more diffuse and less well defined than the leprides of tuberculoid leprosy Macules, papules, nodules, tumours

Untreated lepromatous leprosy, though it may proceed slowly, shows no tendency to spontaneous cure or improvement. Death usually results from intercurrent infections, sometimes from laryngeal stenosis, prolonged reactions or amyloid disease.

Erythema nodosum leprosum (panniculitis nodosa leprosa). This is an acute, subacute or chronic eruption, with or



Fig. 125
Erythema nodosum leprosum.

without fever, of showers of dusky red nodules 0.5 to 2 cm. in diameter on the extensor surfaces of the limbs, the face and less often elsewhere (Fig. 125). There may be a few or hundreds of lesions and some may coalesce to form plaques. The nodules are painful and tender to touch. They erupt quite suddenly and last a week or two to several months. Suppuration is common. Healing usually leaves no scar but hyperpigmentation is common. The general state is little affected.

This eruption occurs only in lepromatous leprosy and is not to be confused with a state of reaction. It may occur in

frequently increase as a result of sclerosis at times when skin lesions are regressing Hypertrophy of nerves is less than in tuberculoid leprosy Eventually all the trophic changes and mutilations seen in tuberculoid leprosy may be reproduced

States of reaction in lepromatous leprosy are more serious than in tuberculoid leprosy There is commonly high fever remitting in the morning headache chills, prostration and



FIG. 24

Lepromatous leprosy before and after treatment with Thiacetazone.

[C D [illegible]]

all the signs of a severe toxaemia Existing skin lesions are aggravated and new ones appear Skin ulcers oedema of the face, hands and feet hypertrophy and neuralgia of nerve trunks joint pains mucosal and ocular lesions and lymphadenopathy are also seen A rare manifestation in reaction is an erythematous necrosing eruption known as *Lucio's reaction* The acute phase of reaction may last for months and if reactions quickly succeed one on the other the patient may rapidly deteriorate and die in cachexia Reactions should not be confused with minor bursts of activity which are short lived and not of such serious import or with the common erythema nodosum leprosum

cent are positive in lepromatous leprosy Bacilli are much easier to identify in skin lesions. The skin is pinched up incised and the sides of the wound scraped or a tiny fragment of skin is excised, macerated and spread on slides. Results are almost always positive in lepromatous and borderline leprosy and frequently so in major tuberculoid leprosy

Histological examination is required in difficult cases, but is not always done as a routine in every case in leprasoria with large numbers of patients.

The lepromin test is used in the differentiation of types and variations in result may indicate how a case is developing The demonstration of sensory changes is important in cases where bacilli cannot be discovered.

Histopathology In lepromatous leprosy a granulomatous infiltrate is found in the dermis and hypoderm. There is some times a free zone separating the infiltrate from the epidermis. The infiltrate consists mainly of histiocytes and lepra (Virchow) cells, which are modified histiocytes, with some lymphocytes, plasma cells and, in older lesions, fibroblasts. Lepra cells are more or less conspicuously vacuolated and often have a foamy appearance. By Ziehl-Neelsen staining large numbers of bacilli can be demonstrated, especially within lepra cells, lying in bundles or large clumps (globi)

In tuberculoid leprosy there are small and large foci of epithelioid cells usually accompanied by lymphocytes and sometimes by Langhans giant cells. Caseation does not occur The infiltrate may come up to the epidermis with no free zone Bacilli are few or absent. Invasion of nerves in the dermis or hypoderm can usually be seen, a point in differential diagnosis from sarcoidosis.

Variable pictures suggestive either of lepromatous or of tuberculoid leprosy are seen in borderline cases bacilli are usually numerous.

A perivascular lymphocytic infiltrate is seen in indeterminate leprosy bacilli are scanty or absent.

Nerve lesions show the same changes as those in the skin. Caseation is common in tuberculoid cases.

Treatment. The introduction of the sulphones has greatly improved the prognosis of leprosy although these drugs are neither curative nor bactericidal. The sulphones assist healing

untreated cases, but is commonest in treated cases, the incidence being in direct proportion to the efficacy of the medicaments used in treatment. It seems probable that it is caused by the products of degeneration of lepra bacilli as it has never been reported in tuberculoid leprosy where bacilli are scanty The term erythema nodosum leprosum is really a misnomer because the reaction is in fact a panniculitis and properly should be called panniculitis nodosa leprosa.

The prognostic significance of the reaction has been disputed *but it now seems certain that it is an unfavourable* sign and one to be controlled rather than promoted

Differential diagnosis The diagnosis of established leprosy in a native of an endemic area presents little difficulty because the observer expects to see the disease but the same native or returned colonial who develops leprosy in Europe or the European developing it in the tropics are very often long misdiagnosed Diseases with lesions resembling those of tuberculoid or indeterminate leprosy include pityriasis streptogenes faciei tinea versicolor tinea trichophytica, vitiligo lupus vulgaris syphilis yaws pinta syringomyelia, Raynaud's disease, porphyria and pellagra. Lesions resembling those of lepromatous leprosy may arise in leishmaniasis, sarcoidosis, the haematodermas and van Recklinghausen's disease

Leprosy is often stated to be a cause for false positive serum reactions for syphilis It should be remembered however that leprosy is common in lands where the treponematoses are usually still commoner False positive tests for syphilis are found in about 15 per cent of cases of lepromatous leprosy but not in cases of tuberculoid leprosy If it is not possible *to resolve doubts by using the treponemal* immobilization test it is wise to treat for syphilis

Diagnosis A positive diagnosis of leprosy is made by demonstrating *lepra bacilli in suitably stained specimens* taken from skin, mucous membrane lymphatic gland or nerve

Nasal scrapings *taken with a curette or by hard rubbing* with a cotton wool-covered probe from the cleaned nasal mucosa, are believed by many doctors to be infallible for diagnosis This is quite erroneous positive *results are few in* indeterminate or tuberculoid leprosy although about 70 per

at least a year in a leprasorium and those with lepromatous leprosy longer Treatment with sulphones continues for two years after disappearance of bacilli in cases of tuberculoid leprosy and for a lifetime in lepromatous leprosy and all cases remain indefinitely under supervision since the only test of cure is time

of lesions repress multiplication of lepra bacilli and cause arrest of the disease in a considerable proportion of cases. The basic sulphone, 4, 4-*diaminodiphenylsulphone* (*DDS*) was synthesized in 1907 but the first use of a derivative (Promin) in leprosy dates only from 1941 Various derivatives and the basic sulphone have since been used but there is no indication that one is better than another and DDS is probably the drug now in commonest use

A daily dose of 0 1 to 0 3 g is given and direct toxic effects are of minor importance Erythema nodosum leprosum is common however and a small number of cases relapse and become refractory to the sulphones

Dihydrostreptomycin (1 g thrice weekly) gives results comparable to those with sulphones but combining the two does not seem to enhance results Other antibiotics are ineffective

Isoniazid sodium para aminosalicylate thiosemicarbazones and chaulmoogra oil are of some value in selected cases

Cycloserine an antibiotic obtained from several streptomyces species is reported to give results comparable to those obtained with DDS It is effective not only in previously untreated cases but also in cases resistant to sulphones. A daily dose of 3 or 4 tablets (0 75 to 1 g) is suggested

Corticosteroids and ACTH are useful in the symptomatic treatment of erythema nodosum leprosum of states of reaction and of ocular complications

The use of BCG vaccine in prophylaxis and treatment has some advocates but there is little concrete evidence of any good effect this treatment is based on the assumption that there exists a cross immunity between leprosy and tuberculosis.

Painful swollen nerves now commonly seen since the advent of the sulphones may have to be incised (neurolysis) and the plastic surgeon can treat mutilations Physiotherapy helps in some cases

The only bacteriological measure of activity of leprosy is the presence or absence of bacilli in the skin and it is the general rule to confine lepers to an institution until repeated skin tests have been negative over a period of at least six months. This means that patients with tuberculoid leprosy will usually spend

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influences. Yaws is believed to have existed in tropical Africa from time immemorial but venereal syphilis was first reported in Europe soon after the return of Columbus from his first voyage to the New World and this was half a century after trade has been established with West Africa. There is still a good deal of argument in favour of the Columbian theory that syphilis existed in the Americas and was introduced to Europe by Columbus's men. The fact that Europeans rarely if ever contract yaws in areas where it is endemic is hard to explain. It may be that they have some natural immunity or perhaps that they live, even in the tropics, under conditions of hygiene and personal segregation vastly different from that of the natives.

Pinta is also a disease of native inhabitants of Central America that is not liable to occur in people of other races, and it is, in its early stages, easily distinguishable from other treponematoses in its late stages a resemblance to yaws may be more marked. Endemic syphilis appears to be identical with venereal syphilis except in its mode of spread and the age of the patients affected the absence of cardiovascular and nervous lesions and congenital disease is especially peculiar here.

Interesting though the problem of the relationships of the treponematoses may be, it is of academic rather than practical interest as all react well to treatment with penicillin, especially the non-venereal diseases.

SYPHILIS

Syphilis is a specific infectious disease caused by *Treponema pallidum* (*Spirochaeta pallida*) It occurs naturally only in the human race, but can be passed experimentally to some animals. Infection occurs directly from person to person in most cases and mediate infection is rare in civilized communities. In congenital or prenatal syphilis the foetus acquires the disease from an infected mother

Syphilis seldom, if ever proceeds to spontaneous cure, but the course of the untreated disease is quite unpredictable and depends on the degree of immunity developed by the patient

CHAPTER XIV

THE TREPONEMATOSES

A VAST number of the world's population particularly in the tropical belt, suffer from one or other of the treponematoses of which yaws and venereal syphilis are the most important and endemic syphilis and pinta of minor importance

All these diseases have features in common and are caused by morphologically identical organisms which must originally have developed from a single ancestral type Although there is a measure of cross-immunity between yaws syphilis and pinta some patients suffering from one can be inoculated with the others The standard serum tests for syphilis and the new treponemal immobilization test become positive in all and offer no help in differentiation

Most of the clinical features of all stages of venereal syphilis are reproduced in endemic syphilis and yaws only pinta has a rather distinctive clinical picture A major difference between venereal syphilis and the other treponematoses is the fact that cardiovascular and nervous lesions are common in the former and very rare, if they occur at all In the latter congenital disease probably occurs only in venereal syphilis.

Venereal syphilis is world wide in distribution yaws occurs only in the native inhabitants of the tropical belt pinta is seen only in Central America and endemic syphilis occurs in confined areas all over the world Apart from venereal syphilis all the treponematoses are diseases contracted mostly in childhood as a result of contact with infected people or by mediate infection The age at onset has been postulated as a reason why major visceral lesions and congenital disease are uncommon in the non venereal treponematoses, but this idea seems unsound when one recalls that neurosyphilis is not uncommon in ordinary congenital syphilis.

It has often been stated that yaws and syphilis are identical any clinical differences being due simply to environmental

A diffuse gummatous process may involve the aorta and other parts of the vascular system including that of the brain. The cerebro-spinal nervous system may suffer as a result of vascular damage or it may undergo gummatous or parenchymatous change more directly Such vascular and nervous affections are rarely diagnosed until about fifteen years after infection.

Such, then, is the picture which theoretically may be seen and typical cases do occur to show all the manifestations described Variations from the typical are the rule, however and whole stages may be missed. A patient may never have any further symptoms after the chancre heals or he may show no secondary signs and after years suddenly develop a gumma or some vascular or nervous manifestation. There is no end to the possibilities.

Fifty years and more ago Boeck of Oslo decided that the natural defences of the body were of more avail in syphilis than the drugs at his disposal. Between 1891 and 1910 some 2,000 cases were kept in hospital until their lesions healed and then discharged with a warning that they would be contagious for another 2 to 5 years. The fate of these patients has been investigated by Bruusgaard in 1929 and again by Gjestland in 1955 many were still alive and autopsy records of others were available. The findings of both investigators were much the same and can be summarized thus. Secondary lesions reappeared one or more times in 24 per cent of cases. Benign tertiary lesions occurred in 16 per cent. Neurosyphilis occurred in 6 per cent tabes, meningo-vascular syphilis and general paralysis were about equally distributed and other types rare Ten per cent suffered cardiovascular lesions. Death was directly due to syphilis in 11 per cent (men 15 per cent, women 8 per cent) but syphilis appears to have a deleterious effect on longevity even when not lethal. Between 60 and 70 per cent of untreated syphilitics go through life with little inconvenience This, however is no argument for repeating Boeck's experiment which took little account of the danger of dissemination of the disease. It has often been stated in the past that the development of skin gummas seemed to protect patients against more serious vascular or nervous lesions, but analysis of Boeck's patients does not bear this out.

against the infection In some cases the forces of immunity may balance against the infection to such a degree that after the early stages a patient may go through a long and healthy life with no evidence of disease apart from positive serum reactions. Acquired syphilis is arbitrarily divided into stages the primary and secondary stages, which are characterized by infectious lesions, are grouped together as early syphilis late or tertiary syphilis is not infectious. The course of untreated acquired syphilis is as follows.

After an incubation period lasting 10 to 70 days (usually about 25 days) *the primary lesion* or lesions, known as *chancres*, appear at the site of inoculation commonly on or near the genitals It has been demonstrated however that *T pallidum* is already widely disseminated throughout the body before the primary sore appears. The chancre heals spontaneously in a few weeks to a few months

Simultaneously or oftener a fortnight to a month or two later signs of the *secondary stage* appear with lesions of the skin, mucous membranes and other organs These lesions, too, heal spontaneously but may recur from time to time over the first 3 to 5 years This period may be regarded as the septicaemic and contagious phase of the disease when *T pallidum* abounds in all the lesions of the skin and other organs. During this time immunity is building up and by the end of the fifth year at latest the character of the disease changes and the tertiary stage begins.

The tertiary stage is one of allergy and the typical lesions, *gummas*, which may arise in any organ, are less widely distributed and show the histological changes of a tuberculoid granulomatous allergic reaction *T pallidum* can seldom be demonstrated in gummas as in all microbic allergides the causative organism is destroyed by the reaction Patients at this stage become non-contagious and are never likely again to develop contagious lesions. Gummas may arise at any time after the start of the tertiary stage, but are commonest from about the tenth year They too, may heal spontaneously but may recur at any time Their importance depends entirely on the organ involved Skin and bone lesions are relatively unimportant though they may be mutilating liver heart or brain lesions may be fatal.

infectious lesions of early syphilis and of early relapsing syphilis are those of the genital region, and in civilized communities syphilis is almost invariably a venereal disease. In some uncivilized communities, however non venereal syphilis is endemic and spreads by ordinary contact especially among children. Extra-genital chancres are generally of venereal origin, but may result from accidental contact in doctors, nurses, etc. Accidental mediate infections on the lips have been described in glass-blowers and musicians and occur in countries where common drinking utensils are used (e.g the *sepours* of North Africa)

In rare cases syphilis has been spread by the transfusion of fresh blood from a donor with early syphilis in such cases there is no chancre of inoculation, but signs of the secondary stage appear after a short incubation period. Laboratory workers handling infected animals or performing the treponemal immobilization test have been affected.

ACQUIRED SYPHILIS

Primary stage

The primary lesion or lesions appear after an incubation period commonly lasting 25 to 28 days during which the patient, although bearing no visible lesions, has been infectious and may have contaminated others. Syphilitic chancres are often solitary but this is not a point to be considered as diagnostically important as they are multiple in 20 to 30 per cent of cases.



Fig. 27
Erosive chancre.

Genital chancres are found in at least 95 per cent of cases. The sites of election in men are the prepuce coronal sulcus, glans or frenum in women the labia, clitoris and vaginal margin.

The pattern of development is upset by inadequate treatment of early syphilis This may produce a state of latency that allays the patient's fears until he develops serious lesions years later Sometimes poor treatment causes the appearance of precocious tertiarism when lesions such as gummas or vascular or nervous involvement begin in the first years or even months of the disease The prognosis of untreated syphilis is better than that of the inadequately treated disease



Fig 126
Circinat syphilide
[illegible]

The course and manifestations of syphilis are to some extent affected by the sex, race and habits of the patient Women are less liable to cardiovasular and nervous syphilis than men The dark-skinned races show more variety than the white in types of secondary syphilitic rashes circinate lesions are far commoner on the black skin than on any other (Fig 126) The negroid races are said to suffer only infrequently from parenchymatous neurosyphilis, especially tabes it must be remembered however that the life span of a tropical negro is not as long as that of a man living in a highly civilized community so that the two are not strictly comparable Moist condylomatous secondary lesions are most frequent in the unhygenic and poor general health, alcoholism and starvation all increase the severity of syphilis at any stage

Congenital syphilis behaves in most respects like a decapitated acquired syphilis beginning in the secondary stage there are, however lesions of the later period which seldom or never occur in the acquired disease

The spread of syphilis In the great majority of cases syphilis spreads directly from person to person The most

The commonest type is the *erosive chancre* This is a painless, round or oval, circumscribed and sharply-edged, shallow erosion. Its base is palpably slightly indurated and its floor is the colour of muscle. It varies in diameter from 2 or 3 mm. to a cm. and may be covered by a thin diphtheroid membrane. Healing usually leaves no scar (Fig 127)

The classical *Hunterian, button or ulcerative chancre* is less common. It is a sharply-defined ulcer with a granulating



Fig. 90
Ulcerating chancre and brawny oedema.
[Wellcome Museum of Medical Science]

floor sometimes covered with a scab The base is indurated and the infiltrated tissue may feel quite cartilaginous when the sore is picked up between finger and thumb Variations in size from a few millimeters to several centimeters are seen (Figs. 128 and 129)

These are the two basic types, but variations are described as dwarf or giant chancres, papulo-erosive, papyraceous (covered with papery scab) penetrating (e.g through the prepuce) phagedenic (widely-spreading and necrotic as a result of secondary infection) mixed chancre (syphilis plus chancroid) etc.

Fig. 128
Ulcerative chancre



Fig. 129
Ulcerative chancre hourglass type



Fig. 31
Erosive chancre.



Fig. 32
Ulcerative chancre.
[*Sydney Thomson*]



Fig. 33
Erosive chancre
[illegible]]

The chancre may be concealed within the meatus or urethra in both sexes and cause only dysuria and a mucoid discharge Chancre of the cervix, erosive or ulcerative, is not uncommon but the vaginal wall is very rarely affected

Syphilis may begin with an erosive balanitis, known as *Follmann's balanitis* and a similar condition of the uterine cervix has been described both are probably precursors of erosive chancres.

Oedema, sometimes massive and brawny is quite often seen with ulcerative chancres in both sexes and may cause phimosis or paraphimosis in men (Fig 130)

The lymphatics of the external genitals and anus in both sexes drain to the inguinal glands which become palpably enlarged in primary syphilis. The glands on one or both sides may be affected and unless secondarily infected are painless, discrete, slide easily under the skin and feel like india rubber The feel is quite characteristic and an experienced venereologist could make a high percentage of correct diagnoses on this sign alone Such glands do not soften or ulcerate With cervical chancres the inguinal glands do not enlarge the pelvic glands affected are not easily palpable

Extragenital chancres are often but not always, due to venereal contact They occur alone or with genital chancres. The *lips* are a commonly affected site and the lesion may be erosive or ulcerated if the latter it is often accompanied by a good deal of oedema of the surrounding skin or of the whole lip Exuberant granulating chancres, sometimes of large size are not uncommon on the lips The submental glands or those in the anterior triangle of the neck are enlarged, sometimes massively enlarged and painless (Figs 131 and 132)

Chancres on the *tongue gums or palate* are usually of the superficial and erosive type Chancre of the *tonsil* is usually ulcerative and covered with a thick white membrane like that seen in diphtheria the tonsil gland in the neck below the angle of the jaw is prominently enlarged (Figs. 133 and 134)

Chancre of the *finger* commonly simulates a chronic paronychia or whitlow and is rarely diagnosed before signs of secondary syphilis appear Typical ulcerative lesions are rarely seen The epitrochlear or axillary glands are enlarged and painless (Fig 135)

suspected. During this test period only saline soaks should be used and antibiotics, with the possible exception of streptomycin whose treponemicidal powers are negligible, must never be given. It is only rarely that it is impossible to demonstrate *T. pallidum* in primary lesions, but when it is technically difficult or impossible easily to obtain a serum specimen (e.g. with phimosis) it may be possible to find the organism in fluid from an inguinal lymph gland.

Serum tests may not be positive in early cases and the ideal is to establish the diagnosis and begin treatment before

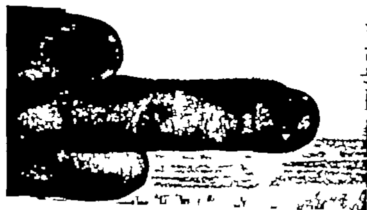


Fig. 35
Chancre of finger

they become positive. In suspect cases serum tests are done systematically every week or two over at least three months if they are consistently negative over this period syphilis is excluded.

Antibodies probably begin to be formed as soon as syphilis is contracted, but their titre does not rise high enough to be estimated in most cases until about two weeks after the chancre appears.

Biopsy should not be delayed if carcinoma is suspected carcinoma in its earliest stage may look very like an ulcerative chancre.

Except at times when or in places where syphilis is prevalent extragenital chancres are usually misdiagnosed until secondary

Chancre of the *nipple* was common in the days of wet nurses, but is now seldom seen except in areas where syphilis is endemic when a mother may be infected by her child

Extragenital lesions of every area from the toes to the scalp have been described

Diagnosis A great deal could be written on the clinical points of difference between syphilitic genital chancre and other



FIG 134
Cervical adenitis with chancre of right tonsil.

erosive or ulcerative conditions such as chancroid scabies, herpes genitalis balanitis, impetigo traumatic ulcer tuberculous ulcer squamous carcinoma etc A certain diagnosis of syphilis is made only on the demonstration of *T pallidum* by dark-ground examination or on serological grounds It is a safe rule to suspect any genital sore of being syphilitic until it is proved otherwise Dark-ground examination of serum from the sore if it does not at once reveal *T pallidum* must be repeated daily for at least three days, and longer if syphilis is strongly

suspected During this test period only saline soaks should be used and antibiotics, with the possible exception of streptomycin whose treponemicidal powers are negligible, must never be given. It is only rarely that it is impossible to demonstrate *T pallidum* in primary lesions, but when it is technically difficult or impossible easily to obtain a serum specimen (e.g with phimosis) it may be possible to find the organism in fluid from an inguinal lymph gland.

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lesions appear. Dark-ground examination is done when syphilis is suspected, but in the case of chancre of the lip the interpretation of the test must be cautious because of the constant presence of non pathogenic spirochaetes in the mouth; the finding of *T. pallidum* in lymphatic gland fluid is not open to this doubt.

Secondary stage

Clinical signs of secondary syphilis usually make their *appearance 2 to 3 weeks after the chancre has erupted.* The chancre may still be active or it may have healed. The vast majority of untreated cases develop signs of the secondary stage within the first six months and the manifestations may disappear and relapse again in the same or in other forms, over the first 3 to 5 years. Sometimes a patient shows signs early in the secondary stage that heal and are not followed by recurrences and very rarely are secondary signs entirely absent. A patient presenting no signs of syphilis apart from positive serum tests during the first 3 to 5 years after infection is termed as suffering from early latent syphilis.

Inadequate treatment in the early stages may induce latency and relapse may take place after months or years with lesions of the secondary or the tertiary types. Whether the patient is treated inadequately or not at all the secondary stage with its possibility of infectious lesions, lasts roughly 3 to 5 years; an exception is that inadequate treatment may speed up the course of the disease so that lesions of the tertiary type appear in the skin or other organs during the time at which only *secondary lesions are normally expected.*

T. pallidum can be demonstrated in all the organs during the secondary stage and may cause a great variety of lesions of which the superficial are the commonest. Mild general *symptoms such as malaise, weakness, indeterminate* joint and muscle pains and headache are often felt and a low fever is not uncommon. Serum tests are always strongly positive by the time signs appear and remain so throughout the secondary stage.

Secondary lesions of the skin occur in about 80 per cent of cases, of the buccal mucosa in 40 per cent, of the nervous system in 10 per cent, of the eyes in 4 per cent; alopecia occurs

in 7 per cent and visceral lesions in 0·2 per cent. There are four cardinal signs of secondary syphilis skin eruptions, mucous patches on the buccal mucosa, condylomata lata and general adenopathy It must be understood that the surface lesions are all basically identical and are modified only by the type of integument on which they arise Secondary syphilides are almost invariably completely symptomless and violent itch is very much against the diagnosis.

CUTANEOUS RASHES

The rashes seen in secondary syphilis are of great variety and can imitate nearly every type of skin disease They are usually macular maculo-papular or papular less frequently pustular Scaling is not uncommon, but vesicles and bullae may be said for all practical purposes not to occur A variety of lesions is often seen in a single case In people predisposed to a chronic skin disease such as psoriasis or seborrhoeic dermatitis the lesions of secondary syphilis are liable to simulate those of the disease from which the person suffers. The skin alone may be involved, but usually there is evidence of involvement of other surfaces or organs.

The *macular syphilide* is the commonest early manifestation and it may remain purely macular or develop later to maculo-papular or papular It consists of a diffuse mottling of rose or ham-coloured, discrete, round or oval macules from 2 mm. to 2 cm. in diameter Pressure with a glass slide blanches the lesions, but they do not fade entirely no infiltration is palpable. The trunk and adjacent upper arms and thighs may be affected, the face less frequently Macular rashes are often faint and fleeting and only perceptible in a good light they fade without trace In other cases the rash is darker and more persistent and leaves a little brownish pigmentation, slow to disappear when the erythema subsides. The eruption often temporarily flares up and becomes redder or darker in colour within a few hours of starting treatment, or a rash may appear only after the first injection has been given to a case of primary syphilis. Drug eruptions and the infectious fevers come most in question in differential diagnosis.

Papular and maculo-papular syphilides are often more wide-spread than purely macular rashes and may affect the face,

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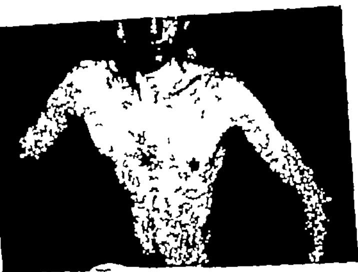
SECONDARY STAGE

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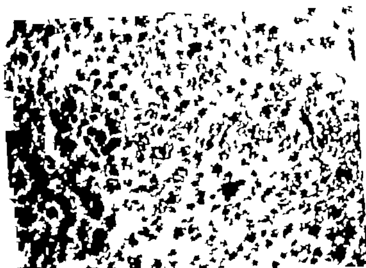


FIG. 98

Papulo-squamous syphilide.

[Sydney Thomas]

Fig. 156

Left. Papular syphilide. *Right:* Lichenoid syphilide

[D. H. Pfeiffer] *[P. W. Hill]*



Fig. 37

Circinate syphilide

D. C. M Arthur

palms and soles. The papules may be small or large, but are generally all of one size. They are indurated and on the palms and soles may feel shotty they range in colour from red to yellowish-brown. The lesions are usually disseminated, but may occasionally be grouped or so arranged as to make circinate or serpiginous figures. Small raised annular lesions up to 1 to 2 cm. in diameter occur in all races but are especially



FIG. 4
Pustular syphilide.

[J. E. Schneider]

common on the dark-skinned races the face and genitals are sites of election. Sometimes the forehead at the hair margin is picked out by papular lesions to produce a *corona veneris* When scaling occurs it is often most marked at the edges of the papules giving the appearance as if the papule had burst through the stratum corneum like a mushroom (Figs. 136 to 140)

The absence of itch and the fact that serum tests are invariably strongly positive distinguish these syphilides from lichen planus, psoriasis, parapsoriasis guttata, pityriasis rosea, acne and the host of other skin diseases that may have to be considered in differential diagnosis.



Fig. 139

Squamous syphilid



Fig. 40

Exuberant papular syphilides

Pustular syphilides are relatively rare, but it is not uncommon to find a few papulo-pustular lesions with a papular syphilide. Widespread small pustular rashes, varioliform syphilides, or eruptions of a smaller number of larger impetigo-like or rupial lesions (covering granulomatous areas) may be seen In the framboesiform syphilide the lesions are red, papular or small nodular masses of soft granulation tissue, and sometimes larger



FIG. 43
Corymbiform syphilide.

W. F[illegible]]

lesions are surrounded by groups of smaller ones (corymbiform syphilides) Pustular syphilides were often seen in Elizabethan times, but today are uncommon in civilized communities except in debilitated people (Figs 141 142 and 143)

Lesions about the face and head may exactly simulate impetigo, and rupial psoriasis, variola, varicella and ecthyma all figure in differential diagnosis. Yaws may come in question in tropical areas, but as treatment for the two diseases is the same the matter is largely of academic interest.



FIG. 142
Rupial syphilide

longer lasting and produce larger lesions than an original roseola. Circinate and serpiginous small papular eruptions confined to the face or genital area are often seen and indolent papulo-squamous eruptions may appear on the palms and soles. Such lesions all teem with spirochaetes and their bearers are fruitful sources for the spread of infection

Transitional syphilides. Towards the end of the secondary stage, or earlier in cases inadequately treated, localized grouped eruptions with characteristics suggestive of both secondary and tertiary syphilis are sometimes seen. A group or groups of papular or small nodular lesions arranged in circinate or serpiginous pattern, slow to heal and tending to peripheral spread is the commonest variety but hypertrophic lesions may occur on the lips. The clinical picture is reminiscent of a gumma, but the history and the finding of *T pallidum* in serum from the lesions shows that the secondary stage has not yet ended although a transition is in progress.

CONDYLOMATA LATA

The surface lesions of moist areas are larger and more exuberant than those on dry skin and consist of reddish-brown to purple, flat topped, oval or circular papules or small, raised plaques that glisten with serum. Sites of election are the glans penis, scrotum and adjacent thighs in men, the labia majora in women and th perianal region in both sexes. The axillae, submammary areas and even th webs between the toes may be affected Exuberant papules or circular plaques t the mouth angles ("split papules) and naso-labial ngles are quite common



FIG. 43
Condylomata lata on thighs, condylomata acuminata on vulva
[H Pfeiffer]

Recurrent syphilides An untreated syphilitic may only once show superficial signs of the secondary stage, but generally there are recurrent eruptions interspersed by long or short periods of latency during the first few years especially in the



Fig 41
Recurrent circinate syphilid

first two years. Recurrent lesions may always take the same form as the original rash in a given patient but on the whole they tend to be more localized and discrete and often appear on the mid line e g on or about the genitals or on the buccal mucosa (Fig 144) Recurrent roseolar rashes are usually

snail-track ulcers Common sites are the fauces and tonsils, uvula and soft palate and the inner surface of the lips, but



FIG. 48
Condylomata lata in recurrent syphilis.

) part of the buccal mucosa may be affected. Similar lesions may arise on the posterior wall of the pharynx, on the nasal

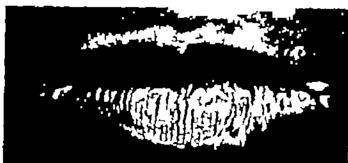


Fig. 146
Split papules in secondary syphilis.



Fig. 147
Condylomata lata. Relapse lesions that appeared six months after treatment of primary syphilis with penicillin.

(Figs 145 and 146) Lack of hygiene seems to be a potent factor in the appearance of condylomata lata especially in areas apart from the genitals.

Condylomata lata may be the only sign of secondary syphilis, but generally they appear along with other skin or mucosal manifestations. Relapse lesions are often fewer and larger than those seen early in the secondary stage and they are not infrequently the only superficial signs of disease they are highly contagious (Figs. 147 and 148)

Mucous patches

Mucous patches are shallow erosions or ulcers, oval or circular in shape with a red floor of granulation tissue which is often covered by a thin white membrane which suggests the other common name for the lesions,

snail-track ulcers Common sites are the fauces and tonsils uvula and soft palate and the inner surface of the lips, but



FIG. 48
Condylomata lata in recurrent syphilis.

any part of the buccal mucosa may be affected. Similar lesions may arise on the posterior wall of the pharynx, on the nasal

mucosa and on the larynx (hoarse voice) The lesions which are seldom solitary vary in size up to 1 or 2 cm but may coalesce to denude larger areas Those on the tongue seldom show a membrane Hypertrophic papular lesions with an eroded surface also occur Deep ulceration is rare and is generally seen on the tonsils if it occurs Healing usually leaves no trace Mucous patches may rarely be the only sign of secondary syphilis they almost invariably accompany skin rashes They are quite frequently a solitary phenomenon in recurrent secondary syphilis and are highly contagious.

ADENOPATHY

A general enlargement of the superficial lymph glands, quite apart from the satellites of the primary sore is a common sign in the secondary stage and may occur without other evidence of disease The glands have the same rubbery consistency as the satellites. Commonly affected are the inguinal post auricular and epitrochlear glands and those in the posterior triangle of the neck The enlargement is discrete and painless and rarely enough to be confused with the lymphadenopathy of diseases of the lympho-reticular system While enlargement of the epitrochlear glands has some significance in diagnosis in the European it means nothing whatever in the South African Bantu where these glands are palpable in 50 per cent of normal subjects



FIG 49
Syphilitic leukomelanoderma
London Hospital

LEUKOMELANODERMA

A reticulate pigmentation enclosing depigmented macules on the sides and back of the neck is sometimes seen in secondary syphilis. Dark haired women are oftenest affected and the change is noted only some 4 to 6 months after infection, but may persist for a long time in untreated cases. Occasionally the shoulders and even the upper arms may be affected. The change may supervene on an earlier eruption, but generally it appears on previously normal skin (Fig 149)

ALOPECIA

A patchy incomplete alopecia of the sides of the head may occur alone or with leukomelanoderma about six months after infection with syphilis. Both sexes are affected but the "moth-eaten" appearance is best seen in men with cropped hair (Figs. 150 and 151) Alopecia areata with its bare areas is not likely to be confused with syphilitic alopecia. The eyebrows, facial and pubic hair may be affected in the same way A generalized, mild falling of hair may also be noted early in the secondary stage

ONYCHIA AND PARONYCHIA

A fairly rare manifestation of the later secondary stage is onychia and paronychia affecting several or all the finger nails. The paronychia is an indolent reddish-brown oedema of the skin, seldom suppurating and often painless, unlike septic infections. The nails are ridged, furrowed or otherwise deformed and break easily or may even be detached. The course is chronic, lasting months or even a year or more.

OTHER SECONDARY MANIFESTATIONS

Affections of the bones and joints, hepatitis (icterus syphiliticus precox) kidney and bladder affections, auditory neuritis, epididymitis, myocarditis and splenomegaly may all occur Iritis is not uncommon and neuroretinitis can be found quite frequently if it is looked for Changes of the meningitic type in the cerebro-spinal fluid, producing no symptoms, may be found in at least 25 per cent of patients and in rare cases basal meningitis, meningo-encephalitis, myelitis and meningo-vascular syphilis occur



Fig. 150

Alopecia in secondary syphilis.

[J. E. Schneider]



Fig. [illegible]

Syphilitic alopecia and pigmenting syphilide

TERTIARY STAGE

The tertiary or late stage of syphilis, which begins between 3 and 5 years after infection, is characterized chiefly by destructive lesions, gummas, resulting from a chronic tuberculoid allergic reaction to *T pallidum*. Signs of late syphilis commonly appear after a period of latency lasting some years but there may in some cases, be an imperceptible alteration of secondary *relapsing manifestations* into tertiary lesions.

We are concerned here only with those lesions which are visible on skin or mucosal surfaces, but it should be understood that the examination of a patient with such lesions is incomplete



FIG. 52
Ulcerative gumma of the chest wall.

if it does not include careful investigations of the state of the cardiovascular and nervous systems and of other organs in some instances.

Gummas of the skin, mucous membranes and bones may arise at any time after about the third year are commonest about the tenth year and rarely appear later than the twenty fifth year after infection. Inadequate treatment of early syphilis may hasten their appearance Gummas are often solitary and are rarely numerous, although they may in some forms, attack large surfaces their distribution is seldom symmetrical as in secondary syphilis Trauma may play a part in their appearance. Untreated, they heal with scar formation after a few months to a year or two. They may be mutilating,



Fig 153
Ulcerative gumma.
[Sydney Thomson]



Fig 154
Ulcerated gumma

but are essentially benign except when, by extension, they affect some vital tissue

The discrete gumma seen on the skin may have arisen in the skin itself or in underlying tissue such as bone, muscle or bursa. There is a certain predilection for the lower limbs, but any part of the skin may be affected. When a gumma begins in skin it is first seen as a firm nodule with a brown to bluish surface. Central softening is followed by ulceration. The ulcer which gradually enlarges in size and may reach quite large dimensions, is roughly round or oval, has a deep, sharp edge and a yellow "wash leather" sloughing base and is surrounded by an areola of induration (Figs. 152, 153 and 154). Deeper tissues such as bone or tendons may be uncovered. Healing leaves an atrophic scar with surrounding pigmentation. Such gummas are frequently solitary. Regional glands are not enlarged.



Fig. 55
Nodulo-ulcerative gummas.
[D. H. Pfleger]

Variants of this type of gumma are sclerotic gummas which do not ulcerate and infiltrated plaques (*gomme en nappe*) that ulcerate in several places like a carbuncle and may eventually denude large areas.

Nodular gummas of the skin are composed of grouped, small coppery or reddish brown, indurated nodules. There may be one or several groups of lesions and in most cases there is a tendency for the nodules to be arranged in circinate, annular or gyrate patterns. The lesions slowly extend, the original nodules



Fig. 156
Nodular gumma.
[Sydney Thomson]

healing with white or pigmented atrophic scarring and fresh nodules appearing around the circumference Healing takes place after months or years during which time very large areas, such as the whole of the back, may have been affected (Figs. 155 and 156)

Superficial scaling over the nodules is commonly seen Pure nodular and nodulo ulcerative varieties are equally common the ulcers are small and discrete and do not tend to denude large surfaces, but they leave considerable scarring

On the palms and soles such gummas may produce a thick hyperkeratosis reminiscent of psoriasis or rarely lesions almost indistinguishable from plantar warts (*clous syphilitiques*)

Lesions of the face may mimic lupus vulgaris, but they spread far more rapidly Occasionally lymphatic obstruction may produce elephantiasic swelling of the lips, ears, genitals or elsewhere. Grave mutilations of the face are seen when both skin and bones are affected (Fig 157)



Fig. 157
Mutilating gumma.
[D H ...]

Other tertiary lesions of the skin include ulcero-

vegetating papillomatous and verrucous gummas and chronic non-infiltrated erythematous macules and plaques. Juxta articular nodes and pinta-like or vitiliginous depigmentation (especially at the extremities) are sometimes seen such lesions are commonest in the dark-skinned races (Fig 158)



Fig. 158
Tertiary syphilis. Pinta-like depigmentation.

The mucous membranes often show gummatous lesions of the discrete type The genitals, lips, palate and tongue are sites of election. Gumma of the genitals may closely resemble primary chancre and it is possible that in some cases at least this is a manifestation of reinfection with *T pallidum* in a person with a degree of immunity *T pallidum* is, naturally not demonstrable by dark-ground examination The tongue may show either



Fig. 159
Gummas of the tongue
[F. B. F. Parr ?]

a solitary gumma or a diffuse sclero-gummatous thickening with lobulation (Fig 159)

Syphilitic leukoplakia affects particularly the lower lip, the cheeks near the angles of the mouth and the tongue, where it may be associated with a sclero gummatous process (Fig 160) Leukoplakia occurs almost exclusively in men It was never a very common manifestation of syphilis but its incidence had begun to decline even before the penicillin era perhaps as a result of rising standards in dental hygiene

In its mildest form leukoplakia produces a uniform whitening of the affected mucosa In more marked degree



Fig. 160
Syphilitic leukoplakia
F. B. F. Parr ?

there is a thickening sometimes considerable and even warty of the mucosa which loses its suppleness and may become fissured

or ulcerated. Squamous carcinoma may supervene. The genital mucosa, including the cervix uteri is rarely affected.

Syphilitic arteritis of the smaller blood vessels is very rare, but may be the cause of gangrene of one or more digits (usually toes)

CONGENITAL SYPHILIS

In congenital or prenatal syphilis the child of a syphilitic mother is infected during intra-uterine life The course of the disease is roughly comparable to that of acquired syphilis without the primary stage There is an early stage with contagious lesions and a late stage with gummatous lesions and also specific lesions which do not occur in acquired syphilis. There are great variations in the pictures produced by prenatal infection which depend to some extent on the stage of syphilis in the mother at the time of pregnancy If the mother has active early syphilis the child is usually born with lesions or develops them shortly afterwards, but if the mother has long suffered from syphilis the child may be born apparently healthy and show signs of late congenital syphilis only after some or even many years. A woman with an old, burnt-out syphilis may produce healthy children. Syphilis may account for stillbirth with a macerated foetus, but is rarely the cause of abortion early in pregnancy

The incidence of congenital syphilis has been enormously reduced in civilized communities where serum tests for syphilis are done as a routine during pregnancy since the advent of penicillin whose use at any stage of pregnancy almost invariably protects the foetus. Penicillin has also greatly improved the prognosis in early congenital syphilis.

Early congenital syphilis

Signs of the early stage may be present at birth or appear soon afterwards. This stage, which lasts about two years, corresponds to the secondary stage of acquired syphilis and serum tests are strongly positive

The child is often puny with a sallow skin, scanty wig-like hair and a general appearance of senility A purulent nasal discharge *snuffles* is often the first overt sign of infection the



Fig 159
Gummas of the tongue
[F W F Purcell]

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Fig 160
Syphilitic leukoplakia
[F W F Purcell]

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common. Less frequent lesions are orchitis, nephritis, hepatitis with icterus, ascites, choroido-retinitis and iritis.

Diagnosis depends on the results of dark-ground examination of serum from lesions and serum tests in mother and child. Difficulties arise when a normal looking child of a recently treated syphilitic mother is found to have serological evidence of syphilis at birth. In such a case quantitative serum tests are repeated weekly at first, later at longer intervals. If the tests show progressive diminution in titre of positivity and eventually (usually in a month or two) become negative it can be assumed that the child is healthy and that the reagin was carried over from the mother. Apparently-healthy children of treated mothers should be followed up with repeated tests for at least a year whatever the result of the first serum test.



FIG. 61

Early congenital syphilis. Circinate eruption.

LATE CONGENITAL SYPHILIS

This stage, corresponding to the tertiary stage of acquired syphilis, begins about the end of the second year but there may be a long period of latency after the early stage or there may be transitional phase when lesions of the early and late varieties are intermingled. In some cases, as already noted, a child will show no early signs, but develop lesions only late in childhood or even in adult life (rarely after the age of 30). Evidence of congenital syphilis may be confined to positive serum tests fortuitously discovered. The lesions of late congenital syphilis may be like those of tertiary acquired syphilis or they may be specific manifestations, the stigmata, existing alone or with the others.

nasal passages may be blocked and give difficulty in breathing and in feeding Destruction of bone may eventually lead to depression of the bridge and saddle-nose

Maculo-papular rashes may appear or recur at any time during the early stage squamous eruptions are rarer Bullae on the palms and soles, arising from an indurated base are strongly suggestive of congenital syphilis such lesions are seen in the early weeks of life Moist condylomatous lesions of the genital and perianal regions are common and often recurrent.



Fig. 161

Early congenital syphilis. Bullous eruption.

Similar lesions may be seen by the mouth and nose (where healing may leave radiating scars rhagades) and in other moist regions. Onychia and paronychia usually of several nails are less common as is patchy alopecia *T pallidum* is easily demonstrable in serum from moist lesions (Figs. 161 and 162)

Enlargement of the liver is common and the spleen is usually enlarged and hard Interstitial inflammation and fibrosis of the lungs pneumonia alba rarely causes clinical signs but is often found at autopsy

The bones are often affected and osteochondritis (epiphysitis) osteitis and periostitis are seen Osteochondritis usually affects long bones and may cause pseudo-paralysis (Parrot) it is often demonstrable on radiological examination. Dactylitis and destruction of the nasal septum are fairly common

Tests show that the nervous system is often involved but clinical signs of meningeal or other involvement are *not*

Interstitial keratitis is one of the commonest manifestations, beginning usually at or after puberty It is often recurrent and resistant to treatment and may lead to grave visual defects or blindness. Eighth nerve deafness is also a late manifestation and with interstitial keratitis and abnormal incisors is included in Hutchinson's triad (Fig 163)

Cutaneous gummas are fairly common, but periostitis, osteitis and bone and joint lesions generally are commoner than in acquired syphilis. Among the lesions produced are anterior bowing and thickening of the tibia (sabre tibia) thickening of the inner third of the clavicle and painless bilateral effusion into the knee joints (Clutton's joints) (Figs. 164 and 165)

Neurosyphilis of all types may occur but cardiovascular lesions are rare.

The late congenital syphilitic is not contagious, but there are rare cases in which it seems probable that a congenital syphilitic mother has infected her children to produce third generation syphilis and treatment during pregnancy is, therefore, counselled.

The diagnosis of syphilis

The two main diagnostic tests used in syphilis are dark ground examination for the demonstration of *T pallidum* and serum tests to show the presence of antibodies. Examination of the cerebro-spinal fluid is important in the investigation of neurosyphilis and biopsy may sometimes be required in gummatous lesions.

Dark-ground examination of serum expressed from a chancre or from a lesion of secondary syphilis in most cases quickly reveals the living moving treponemes and treatment may then begin without waiting for the results of (blood) serum tests. Tests should be repeated daily for several days if no treponemes are at first seen in suspicious lesions. In such cases only saline soaks or dressings are permitted. *T pallidum* can also be demonstrated in serum extracted from enlarged inguinal lymph glands and this is useful when antiseptics have been used on a sore or if there is gross secondary infection with other treponemes which make the identification of *T pallidum*

The child with congenital syphilis may be generally retarded walking late teething late and maturing late Bossing of the frontal bones, scaphoid scapula and a high narrow palatal arch are sometimes seen but alone are not diagnostic.

Characteristic signs may be found in the teeth The permanent upper central incisors may be wedge-shaped

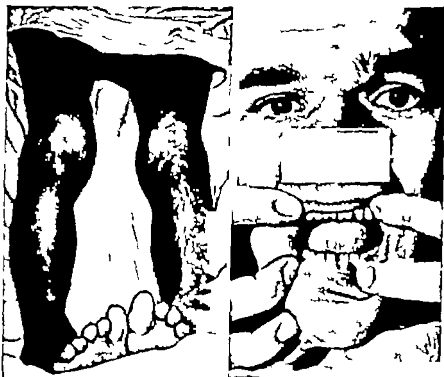


FIG 163

Late congenital syphilis. Clutton joi ts, Hutchinson s teeth and corneal scarring after interstitial keratitis.

thickened antero-posteriorly and tapering from the gum to the free edge which is often notched such are known as Hutchinson s teeth Less often the upper lateral incisors are also affected The first permanent molars may be abnormal and show four small cusps in the centre of a dome or collar of enamel these are known as Moon s or mulberry molars, but are infrequently seen as they usually decay rapidly

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FIG. 164
Late congenital syphilis. Gumma and saddle nose
[Sydney Thomson]

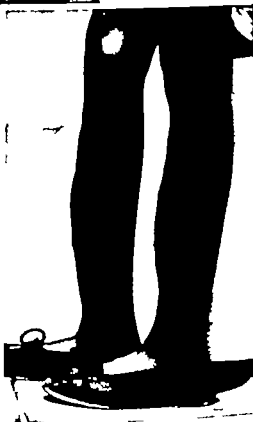


FIG. 165
Late congenital syphilis. Sabre tibia and scars of gummas.
[D. H. Pfeiffer]

difficult. The technique is simple inject about 0 5 cc. sterile saline into the middle of a gland stir the needle about a little and then suck out the mixture and examine treponemes are rarely numerous and a little search may be required, but if any are seen there is no doubt about their nature. Staining techniques to demonstrate treponemes in material from early lesions are of no value as all dead treponemes look alike only the characteristic movements of *T pallidum* distinguish it from other treponemes. *T pallidum* cannot be differentiated even by electron microscopy (which shows it to be provided with flagella) from the treponemes that cause yaws and pinta

Serum tests. The basic reaction, the binding of syphilitic antibody with complement to a non-specific antigen, is the same in the commonly employed complement fixation (Wassermann) and precipitation or flocculation tests (Kline, Kahn, etc.) The formation of antibody probably begins as soon as infection takes place, but demonstrable quantities are found only after about six weeks so that a chancre may have been present for a week or two before serum tests become positive. Although the antigens used are not specifically derived from *T pallidum* the results of tests are remarkably specific in the majority of cases. Positive reactions are obtained in yaws and pinta which are allied to syphilis but false positive reactions may be found with other diseases such as malaria, systemic lupus erythematosus, leukaemia, virus pneumonia, etc., and occasionally for reasons unknown False positive reactions are usually transitory or show fluctuations in titre and it is therefore unwise to make a diagnosis of latent syphilis unless such reactions continue to be strongly positive over a period of some months. This problem has largely been resolved since the introduction of truly specific tests such as the treponemal immobilization test.

Serum tests are always strongly positive in secondary syphilis and generally remain so for the rest of an untreated syphilitic's life but reversion to negative after many years (twenty or more) may rarely occur They become negative after therapeutic cure and the time taken for reversal in early syphilis may be up to a year In cases which are going to relapse an elevation in titre often precedes the return of clinical signs and it is advisable always to use quantitative



Fig. 164
Late congenital syphilis. Gumma and saddle-nose
(Sydney Thomson)

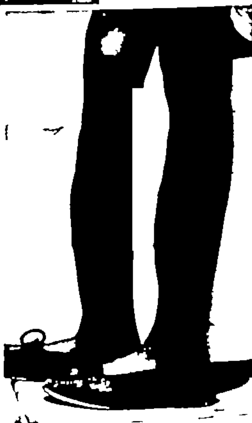


Fig. 165
Late congenital syphilis. Sabre tibia and scars of gummas.
(D. H. Pfeiffer)

tests in the follow up period Reversal to negative is not always obtained after treatment of latent or late syphilis although the titre may drop in such cases no alarm need be felt so long as there are no major fluctuations in titre during follow up and the patient who has been adequately treated may be told that the positive result simply means that he has had syphilis, not that the disease is active. I often employ the simile that a persistently positive reaction is in the nature of a scar

Treponemal Immobilization Test (TPI) Nelson and Mayer have recently elaborated a test founded on the observation that syphilitic serum contains specific antibodies that in the presence of complement, immobilize *T pallidum* The test is remarkably specific and has eliminated most of the difficulties arising from false positive reactions with the older tests it does not however help in distinguishing syphilis from yaws and pinta The TPI test cannot, as yet be used as a test for cure as, in well-established cases, it usually remains positive even after adequate treatment for a lifetime No good quantitative TPI test has yet been evolved

Nelson has also shown that, in a suspension of dead treponemes with syphilitic serum, complement and whole human blood the treponemes disappear The treponemes appear to be sensitized by a specific antibody in the serum react with complement adhere to erythrocytes and be phagocytized by the leukocytes This reaction seems to be as specific as the TPI test and the use of dead treponemes, which can be conserved over some weeks, avoids one of the chief difficulties of the TPI test.

Neither of the above tests becomes positive as early as do flocculation or complement fixation tests in early syphilis. Their use lies in the diagnosis of latent and late syphilis and in clarifying the picture in cases showing false positive reactions with the older tests

Histopathology The basic pathological changes in syphilis are a predominantly perivascular lymphocytic and plasma cell infiltrate endarteritis and endophlebitis and in tertiary lesions, a tuberculoid infiltrate with caseation necrosis Treponemes are demonstrable by special staining techniques in the lesions of early syphilis, but only exceptionally and after prolonged search of serial sections in those of late syphilis.

THE TREATMENT OF SYPHILIS

Soon after syphilis was first recognized in Europe at the end of the fifteenth century mercury was used in treatment and continued to be the mainstay until the discovery of arsphenamine by Ehrlich in the early years of this century Bismuth began to be used shortly afterwards and until 1943 combined arsenical and bismuth treatments were used with the greatest success for all varieties of syphilis. This type of treatment had one serious draw-back treatment had to be prolonged over a period of at least a year to give a high percentage of cures. It was found that rapid arsenotherapy" in which the curative dose was given over a period of from 1 to 20 days was, in early syphilis, nearly as effective as long term therapy but carried a great risk of toxic effects, some of which might prove fatal.

Penicillin was found in 1943 to be spirochaeticidal and effective against human syphilis. The Americans, almost from the first, abandoned other forms of treatment in its favour In Europe there was hesitation and the French especially were inclined to use penicillin rather as a useful addition for the treatment of attack and follow up with other remedies It now appears that penicillin alone is probably as good as penicillin plus other remedies, but there are still competent authorities who prefer to consolidate by giving one or several courses of bismuth injections.

Although nobody would claim that penicillin cures every case of early syphilis (80 per cent is probably a safe estimate) its incomparable advantages are speed of treatment (weeks instead of years) and relative absence of major toxic effects. The greatest drawback of standard arsenotherapy was the fact that comparatively few patients, even in civilized communities, continued to attend for long enough to approach a curative dose.

The more recently discovered antibiotics such as aureomycin, terramycin and chloromycetin are also spirochaeticidal, but have been used only on an experimental scale so that hard and fast rules as to dosage are lacking and they are considerably more expensive than penicillin.

Early syphilis Crystalline procaine penicillin G in oil with 2 per cent aluminium monostearate (PAM) is the preparation most commonly employed at present.

For prophylaxis in a person very recently (within forty eight hours) exposed to infection a single dose of 1 200,000 units PAM is given intramuscularly

For overt primary or secondary syphilis the total dose of PAM is 6 000 000 units given in individual doses of 600,000 units daily or every second or third day depending on the availability of the patient

For patients who are known to be allergic to penicillin and who cannot make themselves available for long term arseno-therapy it may be necessary to prescribe an antibiotic such as aureomycin terramycin or chloromycetin The dosage usually suggested is 60 mg per kilo daily for eight days.

Late syphilis For latent or gummatous benign late syphilis the total dose of PAM is 12 000 000 units given in individual doses of 600 000 units twice weekly

Cases of cardiovascular and neurosyphilis should receive a total of 18 000 000 units of PAM In most types of neuro-syphilis the addition of fever therapy does not seem to increase the number of successes.

Congenital syphilis One of the greatest benefits of penicillin is that treatment of the mother at any stage of pregnancy even in the last weeks, leads almost invariably to the birth of a healthy child a total dose of 9 000 000 units PAM is recommended

Infants with congenital syphilis should be given a total dose of 200 000 units per kilo body weight in divided doses twice weekly Older children may be treated as adults

Relapsing syphilis should first be treated with larger doses of penicillin but if this is not effective one of the old long term arsenic bismuth schedules must be employed

Follow-up A patient with early syphilis must be examined and have a quantitative serum test every month for six months, then every three months for the next eighteen months the cerebro-spinal fluid should be examined at the final test in all cases In cases of late syphilis the scope of examinations will naturally be wider and the length of follow up much greater

Reactions to Treatment

Reactions to penicillin treatment are on the whole mild and unimportant.

About twenty-four hours after the start of treatment of early syphilis with penicillin, as with any potent spirochaeticide, there is often a Jarisch Herxheimer reaction with fever malaise, muscular and joint pains and a flare of any lesions present or even the first appearance of a rash This lasts only for about a day and is presumed to be due to the sudden mass destruction of spirochaetes. It is almost always unimportant, but hepatitis may follow and a crisis of sickling has been reported in negroes with sickle-cell anaemia.

Therapeutic shock as a result of reactionary swelling of lesions is, theoretically a more serious problem when potent drugs are used in late syphilis. The possibility of sudden death from coronary occlusion in aortitis has to be considered. Such catastrophes are, fortunately extremely rare but they do occur and can be prevented by preliminary treatment, for a month or two, with bismuth and iodides.

Therapeutic paradox, the worsening of symptoms in cases of cardiovascular and other forms of visceral syphilis as a result of rapid healing of lesions, can also be avoided to some extent by preparatory treatment with slowly-acting remedies before penicillin is used

Minor allergic reactions to penicillin itself should be treated with antihistaminics, major reactions with ACTH or steroid hormones. These latter substances promote healing of the lesions at all stages of syphilis, but have no curative effect whatever

YAWS

Yaws (pian, framboesia, bouba, etc.) is a very common non-venereal treponematosis of tropical regions. Spread generally occurs by close contact, but a fly *Hippelates pallipes*, has been incriminated as a vector in some cases. Children are affected far oftener than adults. Yaws is almost entirely a disease of the native inhabitants of endemic areas, and Europeans living in the tropics are very rarely infected The course of the untreated disease is similar to that of syphilis except that mucous patches and alopecia are very rare in the secondary stage and cardio-vascular and nervous lesions do not seem to occur congenital yaws is unknown. The causal organism, *Treponema*

For prophylaxis in a person very recently (within forty eight hours) exposed to infection a single dose of 1 200,000 units PAM is given intramuscularly

For overt primary or secondary syphilis the total dose of PAM is 6 000 000 units given in individual doses of 600,000 units daily or every second or third day depending on the availability of the patient

For patients who are known to be allergic to penicillin and who cannot make themselves available for long term arsenotherapy it may be necessary to prescribe an antibiotic such as aureomycin terramycin or chloromycetin The dosage usually suggested is 60 mg per kilo daily for eight days

Late syphilis For latent or gummatous benign late syphilis the total dose of PAM is *12 000 000 units given in individual* doses of 600 000 units twice weekly

Cases of cardiovascular and neurosyphilis should receive a total of 18 000 000 units of PAM In most types of neurosyphilis the addition of fever therapy does not seem to increase the number of successes.

Congenital syphilis One of the greatest benefits of penicillin is that treatment of the mother at any stage of pregnancy even in the last weeks, leads almost invariably to the birth of a healthy child a total dose of 9 000 000 units PAM is recommended

Infants with congenital syphilis should be given a total dose of 200 000 units per kilo body weight in divided doses twice weekly Older children may be treated as adults

Relapsing syphilis should first be treated with larger doses of penicillin but *if this is not effective* one of the old long term arsenic bismuth schedules must be employed

Follow-up A patient with early syphilis must be examined and have a quantitative serum test every month for six months, then every three months for the next eighteen months the cerebro-spinal fluid should be examined at the final test in all cases. In cases of late syphilis the scope of examinations will naturally be wider and the length of follow up much greater

Reactions to treatment

Reactions to penicillin treatment are on the whole mild and unimportant.



Fig. 67
Yaws. Primary lesions in woman infected by her grandchild.
[*W. van der Meulen*]



Fig. 68
Yaws, secondary stage. Framboesiform eruption.
[*W. van der Meulen*]

pertenue can be demonstrated in serum from early lesions by dark-ground examination and the serum tests used for syphilis are positive.

PRIMARY STAGE

After an incubation period of 12 to 20 days the primary lesion or mother yaw appears it arises on exposed skin in



FIG 166
Yaws. Primary lesion.
[*H. van der Merden*]

most cases A mother may be infected by her child the sore appearing on the nipple or elsewhere. The lesion is at first papular or papulo-vesicular becomes scabbed and spreads to form a granulating ulcer up to a few centimeters in diameter Fungating and papillomatous lesions are also seen and the *primary lesion* tends always towards vegetation and proliferation rather than towards rapid spontaneous cure (Figs. 166 and 167)

SECONDARY STAGE

The secondary stage characterized by itchy skin lesions, starts a few weeks *after the primary lesion appears and* while this latter is in full activity Roseolar rashes occur but are hard to see on the black skin Depigmented macules papules scaly papules or macules (yaws trash) and pustules may be seen scaling reminiscent of trichophytosis often occurs on the palms and soles *Later after such rashes or without their*

FIG. 70
Yaws, tertiary stage

[H. van der Meiden]



FIG. 71
Yaws, tertiary stage. Juxta-articular nodes.

[[illegible]]

having been seen begins the characteristic framboesiform (raspberry like) eruption of large exuberant moist and purulent crusted granulomatous lesions (Figs. 168 and 169). Such lesions are especially numerous in moist skin folds where they are comparable to the condylomata lata of syphilis; they heal eventually often with scarring. They are the commonest



FIG 169

Yaws, secondary stage. *Left.* Framboesiform eruptions. *Right.* Crab yaws.
[*W. van der Meer*

lesions of the secondary stage but rashes like those seen in secondary syphilis also occur. Relapsing secondary rashes are often circinate (ringworm yaws). Periostitis is a late secondary phenomenon as is *crab yaws* a very painful ulceration and fissuring of the soles.

TERTIARY STAGE

The tertiary stage begins after a few years, either after a period of latency or imperceptibly supervening on the secondary stage. The lesions include gummatous nodules and spreading ulcers, periostitis and endosteal gummas, tenosynovitis, onychia and hyperkeratosis and fissuring of the palms and soles. Patchy vitiliginous depigmentation of the skin may occur and juxta-articular nodes, small and large fibrous nodular swellings near the elbows, knees and other joints, are fairly common.





FIG. 73

Pinta. *Top*: Primary lesion. *Bottom*: Late blue discoloration of face and arms.

[[illegible] *Marquez*] [Orlando Canizares]

U

both these phenomena are also rarely seen in syphilis and are not diagnostic of yaws though they are very suggestive (Figs. 170 and 171)

Goundou is due to an osteitis beginning in the nasal processes of the superior maxillae that causes at first hard, bean like swellings on the sides of the nose later gross swellings that obstruct breathing and may even encroach on the orbits.



FIG. 172
Yaws tertiary stage. Gangosa.
[E. E. Waller]

Gangosa is a gummatous process that first destroys the soft palate and spreads to involve the hard palate nasal bones and surrounding soft tissues producing horrifying mutilations (Fig 170)

Treatment All the remedies effective against syphilis are even more effective against yaws. A course of eight daily injections of 600 000 units of penicillin (PAM) would normally be used for early cases longer courses or repeated courses are sometimes necessary for late yaws For mass treatment in endemic areas good results are obtained with single injections of as little as 1 200 000 units of penicillin affected and apparently unaffected natives must be treated

PINTA

Pinta (*carate mal del pinto*) is an endemic non venereal treponematosis of Central America that affects negroes and native Indians, but rarely whites. The causative organism, *Treponema carateum* or *T herrejoni* is indistinguishable from *T pallidum* and infected patients develop serum antibodies that give positive reactions with all the tests used in syphilis, but there is no absolute cross immunity between the two diseases. The disease is usually contracted by children between 10 and

on the face, shoulders and extremities (white pinta) (Figs. 174 and 175)

These dyschromic lesions are characteristic of the *late stage* but recurrent blue pinta lesions may still appear as well



Fig. 75

Pinta. Characteristic triangular depigmentation at wrists in late stage.

Orlando Canizares

Hyperkeratosis of the palms and soles, bone pains and juxta articular nodes may occur The question as to the occurrence of major visceral lesions is not settled, but congenital pinta does not occur

Treponemes are to be found in lesions at all stages, an important point of distinction from syphilis and yaws. Serum tests for syphilis become positive a few months after infection. The disease is unsightly but has no major effect on health.

Treatment is as suggested for yaws and is most effective. Pigmentary changes, however are likely to be permanent.

15 years of age by direct contact or possibly as a result of bites of flies of the genus Hippelates

The primary lesion, on exposed skin is usually a small patch of erythema and scaling sometimes a cluster of little papules, that appears 7 to 20 days after inoculation (Fig 173)



Fig 74

Pinta. Hyperpigmentation and depigmentation in the late stage

Orlando Canizares

The secondary stage begins after a few months with similar scaly patches near the primary lesion dissemination of the rash follows Later still appear the characteristic secondary lesions, small and large patches of pink red violaceous and leaden-blue colours that unite to form great polycyclic plaques (blue pinta) Such lesions, as they mature become either brownish or depigmented and a picture like vitiligo appears, especially

ENDEMIC SYPHILIS

In certain areas throughout the world are found cases of an endemic treponematosis which resembles syphilis rather more than yaws. The disease spreads usually among children by contact or as a result of using infected drinking utensils, etc. Various names are used for the condition: the best known is *bejel* (Syria, Iraq) and it is called *njovera* in Southern Rhodesia, *dichuchwa* in Bechuanaland.

Primary sores are rarely seen and endemic syphilis often presents with lesions of the buccal mucosa and condylomata lata



FIG. 77

Endemic syphilis (dichuchwa). Mucous patches.

[J. Murray, Bulletin of the World Health Organization]

in moist skin folds. Disseminated rashes and adenopathy also occur and this stage lasts about a year and is then followed by a spell of latency lasting sometimes for many years. Late lesions include muco-cutaneous and osseous gummas and plantar hyperkeratosis. Juxta-articular nodes, gangosa and goundou-like lesions of the nose and face, alopecia and pigmentary changes may occur (Figs. 176, 177, 178 and 179). Cardiovascular and nervous lesions and congenital disease are said to be exceedingly rare if they occur at all.

In areas where early endemic syphilis is very common, skin gummas are also common. It has been suggested that some, at



FIG 76

Endemic syphilis (dichuchwa)

Top Papular syphilide *Bottom* Condylomata lata.

[*J F Murray* Bulletin of the World Health Organization]

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Fig. 177
Endemic syphilis (dichuchwa). Mucous patches.
(J. F. Murray, Bulletin of the World Health Organization)

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FIG 178

Endemic syphilis (dichuchwa) Hyperkeratosis of soles in early stage

[J F Murray Bulletin of the World Health Organization]



Endem phili dichuchw (umma

J F Murray Bull n of he World Health

least, of the gummas are due to superinfection in untreated cases. The same phenomenon has been noted in yaws. A woman infected by her child at the breast will develop a primary lesion containing treponemes if she herself is free of



Fig. 180

Endemic syphilis. Ulceration followed the suckling of child with buccal mucosal lesions. The mother was seropositive and gav. history of [illegible] in childhood.

(J. F. Murray Bulletin of the World Health Organization)



Fig 181

Witkop.

(J. Murray Bulletin of the World Health Organization)

disease, a gummatous lesion free of demonstrable treponemes if she has had the disease in the past (Fig 180)

Irkulja, a treponematosis of Australian aborigines, is thought by some to be a variety of yaws, by others to be an endemic syphilis. Early lesions are inconspicuous and most cases present with gummatous lesions of skin and bone, often with prominent sabre tibia (boomerang leg)

Witkop is a condition seen in young Bechuanas with syphilis (Fig 181) The scalp is covered with a thick, white, psoriasiform scale The condition lasts for years and is often followed by atrophic scarring and alopecia (kaalkop) It had long been

thought that witkop was a specific manifestation of syphilis but it now seems clear that it is endemic favus in sufferers from endemic syphilis It is not known whether the syphilis acts as a facilitating factor or is purely coincidental.

Treatment as for acquired syphilis is curative and endemic syphilis seems to be more sensitive to penicillin than is the acquired form

CHAPTER XV

VIRAL AND RICKETTSIAL DISEASES

Viruses and rickettsiae (and the related chlamydozoaceae) cause a variety of common and rare diseases affecting the skin and mucous membranes in man.

Viruses are obligatory intracellular parasites containing no energy producing enzymes. The smallest (plant) viruses appear to consist of single large molecules of ribonucleoprotein, but larger viruses may contain also such components as phospholipid carbohydrate and copper. Pathogenic viruses vary in size between 0·01μ (foot and mouth disease) and 0·3μ (molluscum contagiosum).

The rickettsiae are larger than viruses (0·475μ) and contain some simple enzymes, but propagate only within the cells of a host. Related to the rickettsiae are the chlamydozoaceae (0·3 to 0·4μ) which also seem to have some primitive enzyme system and appear to reproduce by binary fission.

Viruses do not reproduce themselves like bacteria, but it has been suggested that they induce infected cells to manufacture their components instead of, or as well as, their own and eventually synthesize new virus particles. In some diseases the multiplication of virus particles produces new structures, inclusion bodies, within the nucleus or cytoplasm of the host cells. these inclusion bodies may consist largely of virus material or of a matrix derived from the host cell.

Viruses frequently produce lesions at the site of inoculation on the skin or elsewhere and spread thereafter may take place over the surface or *via* the lymphatics or the blood stream. Some viruses produce lesions only on the surface (e.g. warts) others usually spread within the body to a limited degree (e.g. milker's nodules) and others still invariably cause a viraemia (e.g. varicella).

Infection with most viruses usually tends to the development of a specific immunity which may, in some conditions, be

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affected (Figs. 182 and 183) In many cases the area to be affected itches and burns for a few hours or longer before there



Fig 82
Recurrent herpes simplex

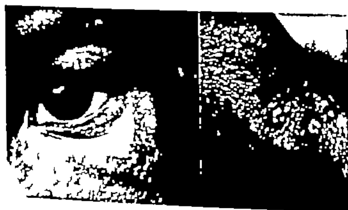


Fig 83
Recurrent herpes simplex of cheek and hand

ppears a slightly oedematous patch of erythema on this erupt groups of closely-set vesicles that dry off to crusts in a few days If

demonstrable by serum or skin tests. In many and sometimes most cases of some virus diseases such as herpes simplex immunity is developed as a result of subclinical or inapparent primary infections

The surface lesions produced by viral and rickettsial infections are of great variety and include an assortment of erythemas vesicles, pustules and tumours The vesicle in viral diseases is characteristically intra-epidermal and results from reticular and ballooning degeneration with acantholysis. Allergides (virides) are seen in some cases

The viral infections are unresponsive to the modern antibiotics which are often most effective against the rickettsial diseases The immunity of the virus is evidently due to the fact that it has no enzyme system which can be blocked ACTH and corticosteroids have little place in the treatment of viral diseases

HERPES SIMPLEX

Herpes simplex (cold sores fever blisters) is one of the commonest viral infections and apart from the banal manifestations, is now known to cause a variety of other lesions The majority of people are infected in childhood the infection being subclinical in 99 per cent of cases, and thereafter harbour the virus and have demonstrable specific antibodies in the blood Primary lesions are rarely seen and were until recently not recognized as being due to herpes virus

The easily recognized *recurrent herpes simplex* occurs in immune persons as a result of certain stimuli which upset the virus antibody balance These stimuli include fever sunshine gastro-intestinal upsets mechanical trauma ingestion of a substance to which a person is allergic, and possibly emotional upsets. Women may suffer regularly recurrent attacks in relation to the menses

Recurrences may be frequent or rare and occur always on the same site or affect different areas Few people never have an attack of herpes An attack can be induced in a previously affected site by the injection of histamine or acetylcholine

Sites of election are the mucocutaneous junctions of the mouth nose eyes, penis and vulva, but any area may be

be very ill with high fever regional adenopathy and in infants, dehydration and acidosis. Recovery takes 10 to 14 days.

Acute herpetic vulvo-vaginitis produces a comparable picture (Fig 184) Rarely a primary infection takes place at a site of trauma on any part of the skin. Kaposi's varicelliform eruption may be due to the virus of herpes.

Primary infection may also take the form of a meningo-encephalitis this may be fatal, but there are no residual changes in those who recover Kerato-conjunctivitis of a severe nature may also be a primary lesion.

Visceral herpes simplex is a rare and fatal disease of infants, often of premature infants, who develop a viraemia and necrotic lesions of the organs. Older children may develop viraemia and visceral lesions with gingivo-stomatitis.

Histopathology The vesicle of herpes is intra-epidermal and due to necrosis of cells balloon cells are seen. There is a polymorphonuclear infiltrate in the underlying dermis and these cells soon invade the vesicle cavities.

Treatment. The common cold sores should be treated with calamine lotion or if they become impetiginized, with 3 per cent aureomycin ointment. In cases where there are frequent recurrences *in situ*, x-ray therapy often gives long spells of freedom. There is no cross-immunity with vaccinia so that serial vaccination is worthless.

Severe primary infections have to be treated symptomatically and corticosteroids are contra-indicated as they appear to worsen the condition.

KAPOSI'S VARICELLIFORM ERUPTION

This disease (which is also described under a great variety of titles such as eczema herpetiforme, herpes vacciniformis, etc.) affects patients, usually children, already suffering from some widespread itching disease such as infantile eczema. It is caused by super infection with the virus of herpes simplex or of vaccinia and the clinical picture is the same in both cases. Special studies are sometimes necessary to identify the cause. The prognosis is poor in cases of primary herpetic infection,

not secondarily infected Healing is complete in 7 to 10 days and scar formation is unusual except in cases where lesions frequently recur on the same site in such cases post inflammatory pigmentation may also occur

Large plaques resembling zoster may be seen usually on the thigh or inguinal region. A rare sequel to an attack of herpes simplex is erythema multiforme presumably an allergide.



Fig. 184
Primary herpes simplex
(R T Bear)

The eye is often affected with keratitis or kerato-conjunctivitis vesiculation and ulceration may occur but *permanent damage is rare unless steroid hormone therapy* is used

Differential diagnosis presents little difficulty except on the genitals where vesicles quickly break leaving little circular erosions that may suggest primary syphilis.

Primary herpes simplex usually occurs in children between 2 and 5 years *old and the commonest form is* acute herpetic gingivo-stomatitis. The disease begins suddenly with very painful white plaques that go on to ulceration Spread may involve the *whole buccal mucosa. The* patient may

be very ill with high fever regional adenopathy and, in infants, dehydration and acidosis. Recovery takes 10 to 14 days.

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(E. T. Ihem)

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VARICELLA AND ZOSTER

It is now generally accepted that varicella (chickenpox) and zoster (shingles) are both caused by one virus. The position is in some ways analogous to that in herpes simplex varicella can be considered as the primary infection, zoster the recurrent disease in an immune person. Zoster has been seen to follow a variety of stimuli, e.g cancer of the breast, leukaemia and Hodgkin's disease, radiotherapy arsenotherapy lumbar puncture, operations (on the Gasserian ganglion, etc.) and other traumata.

Young (non-immune) children develop chickenpox after inoculation with zoster vesicle material, but experiments directed at the reproduction of zoster itself have so far proved unsuccessful. Cross-immunity between the two diseases has often been demonstrated in the laboratory

VARICELLA

Varicella is a common infectious disease of early childhood (1 to 5 years) but may occur at any age from infancy (mother usually affected at time of delivery) to old age After an incubation period of 9 to 21 days the disease begins with a day or two of malaise and fever followed by a rash of tense, clear superficial vesicles on an erythematous, non-indurated base. Fresh lesions appear in crops for the next 2 to 7 days so that various stages of development are visible at the height of the disease The vesicles become cloudy and then dry up to a brownish crust that falls off after about a week. Vesicular erosive or ulcerative lesions of the bucco-pharyngeal mucosa are common and the ocular conjunctiva may be similarly affected. Scarlatiniform rashes may precede the crops of vesicles. Purpuric lesions rarely occur

The disease is usually mild, but it may be severe and complicated in adults, and fatal, with visceral lesions, in infants. Pneumonia, meningo-encephalitis and lesions of other organs have been reported.

The histological picture is the same as that of herpes simplex.

Treatment is purely symptomatic and the patient can be considered non-infectious by the time all the lesions have dried up completely

but much better in those who have already developed immunity in the latter it may even be mild and recurrent. Vaccinial cases (*eczema vaccinatum*) may be due to actual vaccination or to contact with a recently vaccinated person (Fig 185)

The disease begins suddenly with high fever and oedema of the face and sometimes other areas on which appear crops of



Fig 185

Kaposi's varicelliform eruption. Eczema vaccinatum following vaccination [illegible] child with scabies.

varicelliform pustules that often unite to form large suppurating plaques. Ulceration and gangrene may follow The regional glands are enlarged and there is grave toxaemia

Pyoderma and smallpox have to be considered in differential diagnosis in rare cases cutaneous diphtheria may produce such a picture

Treatment is purely symptomatic and the outcome depends largely on the age of the child and the extent of surface affected

ulcers that heal, leaving white scars or areas of depigmentation with hyperpigmented borders. Regional adenopathy is usually found. The affected area may remain painful and tender as long as the rash persists, but it usually returns to normal soon



Fig. 87
Zoster

[P. W. [illegible]]

after healing in young subjects. severe, persistent neuralgia is an important complication of zoster in old people

It is not uncommon to find a few scattered varicelliform vesicles on skin remote from the affected zone, and sometimes there are enough to suggest that the patient has varicella as well. Haemorrhagic vesicles are not uncommon and gangrenous lesions may occur usually in old and feeble patients.

Zoster

Zoster is less common than varicella and occurs mostly in adults, with peak incidence about the age of thirty The lesions are found on skin areas corresponding to the distribution of nerves from one or more posterior root ganglia or of cranial nerves and they are almost invariably unilateral The commonest site is the thoracic region where a band like area



Fig 186
Zoster

corresponding to the distribution of an intercostal nerve is affected Next in frequency are the cervical *trigeminal* lumbar and lumbo-sacral nerves Whether the process begins in the skin or in the nervous system is not yet known

The first signs often preceding the rash by a few days, are burning or pricking pain or itch in the area to be affected and test may show that the skin is *hypo- or hypersensitive* The eruption begins as isolated slightly elevated erythematous plaques that usually extend and flow together On this base form vesicles or even small bullae full of fluid that is clear at first but later becomes turbid (Figs 186 and 187) Crusts form and when they fall after a week or so often leave erosions or

SMALLPOX, COWPOX AND VACCINIA

It is now generally recognized that the diseases in this group are caused by three distinct viruses that may well have developed from the same stem.

Smallpox

Strains of smallpox virus of different degrees of virulence occur in nature and cause epidemics of diseases differing enough in character to allow classification into classical smallpox (variola major) and alastrim (variola minor) The modified disease in vaccinated people is known as variloid



Fig. 188

Smallpox

[illegible]

Classical smallpox begins after an incubation period of 6 to 22 days with a prodromal stage lasting 2 to 3 days and characterized by high fever malaise and vomiting and, sometimes, a fleeting erythematous rash. As the true rash appears the fever drops and the patient feels better this is sometimes a sign of diagnostic importance. The rash is at first papular and most of the elements are on the face and extremities, especially at pressure areas such as the palms and soles the trunk is less affected than in chicken pox. Vesicles form on the papules and by the sixth to the tenth day develop into pustules and there is a secondary rise in temperature The lesions are hard and shotty and usually umbilicated (Fig 188) Crusting appears at the tenth day or soon after Unlike

Abnormalities in the cerebro-spinal fluid are stated to occur in up to 50 per cent of cases protein is moderately increased and abnormally large numbers of lymphocytes and polymorphonuclear leukocytes are found, but these changes are rapidly reversible

All the cranial nerves except the optic and olfactory may be affected The ophthalmic branch of the trigeminal nerve is attacked frequently and the ocular conjunctiva may be affected, occasionally with such grave consequences as keratitis, iritis and even perforation pain is generally severe In the Ramsay Hunt syndrome (geniculate ganglion) the eruption is on the ear and anterior two-thirds of the tongue homolateral Bell's palsy precedes or accompanies the rash and there may be vertigo and interference with taste and lacrimation The auricle, soft palate uvula, tonsil and postero-lateral surface of the tongue are affected if the glossopharyngeal ganglion is involved. When the vagus and its connections are affected the eruption is on the auricle the base of the tongue epiglottis, arytenoids and aryepiglottic folds.

Muscular weakness and transient paresis occasionally occur in any area Alopecia temporary or cicatricial and permanent, may follow scalp lesions In rare cases the attack may be abortive with pain but no vesicular rash later the area shows a temporary hyperpigmentation

The histological picture is as in herpes simplex and varicella with intradermal vesicles and degenerate balloon cells. It is said that the polymorphonuclear cells invading the vesicles are more often eosinophils than is the case in varicella, suggesting that zoster may be an allergic response to infection in an immune subject. Inflammatory and degenerative changes occur in the posterior root or cranial ganglia in the peripheral nerves and even in the posterior columns of the cord

Treatment There is no specific for zoster and antibiotics do no more than control secondary infection Salicylates and codeine best control the neuralgia and calamine lotion is as good an application as any Ocular complications must receive specialist attention Various neurosurgical procedures have been advised for the chronic severe neuralgia that sometimes follows an attack but the results are not often gratifying

The common vaccination reactions will not be described. Accidental vaccination is reasonably common as a result of contact with a recently vaccinated person, and Kaposi's varicelliform eruption is sometimes due to vaccinia virus. Children with eczema or any other itchy dermatoids should be vaccinated only in emergency and must be kept from contact with recently vaccinated people.

Generalized gangrenous vaccinia as a result of chronic viraemia is a rare consequence of vaccination in a normal person who builds up no antibodies the condition may persist for months and is often fatal. Fleeting erythematous rashes about ten days after vaccination are more frequent, but unimportant. Postvaccinial encephalitis is a rare and serious complication that usually follows primary vaccination done after the early years. Erythema multiforme is an uncommon sequela of vaccination.

There is a large measure of cross-immunity produced by infections with the three virus types discussed and control of smallpox depends on the immunization of populations by vaccination. Protection begins 8 days after vaccination and lasts for 5 to 7 years Smallpox cases must be isolated and contacts quarantined for 16 days from the last exposure or until the peak of successful vaccination There is no specific treatment, but antibiotics reduce the risks and consequences of secondary infection.

THE EXANTHEMAS CAUSED BY VIRUSES

The common exanthemas will merit only short descriptions to serve as a reminder for differential diagnosis. It should be remembered, however that there are many cases of exanthematous diseases in children which cannot yet be classified Some may well be atypical forms of common diseases, others are probably separate entities, behaving like virus diseases, that in time and with further observation will be categorized. Variants of the poxes have been noted and epidemic follicular keratosis may be of viral origin. This latter disease is characterized by an erythematous rash followed by comedo-like lesions and small epidemics have been seen in several countries.

chickenpox, all the lesions are in the same stage of development at a given time The buccal mucosa is affected.

Haemorrhagic lesions may be superimposed or the disease may be fulminating and haemorrhagic from the start (black smallpox) The mortality rate for both of these forms is about 80 per cent compared with 10 per cent in discrete and 50 per cent in confluent smallpox Complications include secondary infections corneal ulcers and rarely encephalitis.

In *alastrim* the prodromal stage is milder than in true smallpox and the rash is more discrete on the black skin the lesions look chalky *The mortality is very low except in rare* haemorrhagic cases

Varioloid is also a mild disease of people partially protected by vaccination The course is similar to or even milder than, that of alastrim An unprotected person infected by a case of varioloid will however develop virulent variola.

The diagnosis of smallpox is easy in an epidemic but in isolated cases the help of a virologist may be required

Cowpox

The cowpox of Jenner's time is no longer the commonest pox of cattle The disease of the udders now usually seen produces milker's nodules in man and is due to an entirely different virus Genuine cowpox still does occur however and may pass to man (usually milkers) producing lesions of the backs of the hands, forearms or face The lesion is a domed, reddish blue nodule enlarging to the size of a pea, painful, firm and elastic and surrounded by woody oedema There is usually lymphangitis and regional adenopathy and sometimes a generalized erythematous rash on the extremities. Suppuration often occurs and is followed by ulceration that is slow to heal

Vaccinia

The vaccinial virus used today is entirely different from that which causes cowpox It may be a mutant from cowpox or have resulted from contamination in earlier days when cowpox vaccination was done from man to man at times when smallpox was prevalent.

and nephritis and conjunctivitis may occur. Meningeal symptoms and meningo-encephalitis are rare.

In the early stages there may be leukopenia, but when the disease is fully developed there is a leukocytosis to as high as 80,000 cells per cu. mm. Monocytes and large lymphocytes are increased while polymorphonuclear leukocytes are relatively and absolutely reduced. The serum may give temporary false positive reactions for syphilis and it contains a heterophile antibody causing agglutination of sheep red cells (Paul-Bunnell test).

The disease may end in a few weeks or persist in chronic relapsing form for months.

DENGUE

This is an epidemic mosquito-borne virus disease of tropical and sub-tropical areas. Monkeys are naturally infected and serve as jungle hosts.

The incubation period is 2 to 15 days. Some cases begin suddenly with fever, chills and malaise; others begin gradually with headache, malaise and, sometimes, flushing of the face and a punctiform rash most marked at friction points. Later comes high fever and severe joint and muscle pains (breakbone fever). The fever lasts 5 to 6 days and the patient is left exhausted. A secondary maculo-papular or scarlatiniform rash often appears about the third to fifth day, first on the body and later spreading to the face and limbs. Petechial purpuric spots may appear on the extremities, axillae and buccal mucosa at the end of the fever. There is usually generalized adenopathy and sometimes splenomegaly. The blood picture is of leukopenia with relative lymphocytosis.

Recurrent attacks may occur, probably as a result of infections with different strains of the virus. Treatment is non-specific but there is an effective vaccine (Sabin's).

HERPANGINA

This is one of the clinical syndromes which are caused by certain strains of Coxsackie virus; other manifestations of

MEASLES

The incubation period is 12 to 14 days. The disease begins with fever coryza and conjunctival congestion The temperature rises on the first day, often falls on the second to rise again on the third day and stay elevated until the rash is out. Koplik's spots bluish white on a bright red base are found on the buccal mucosa at this time

The rash starts on the fourth day on the brow and behind the ears it becomes generalized within twenty four hours. It is dark red and maculo-papular and the lesions tend to fuse to irregular blotches Small vesicles may be seen and a little scaling is evident after a few days

GERMAN MEASLES (rubella)

The incubation is 14 to 23 days and the disease begins with low fever and perhaps a little conjunctivitis. The rash begins on the forehead and behind the ears and then becomes generalized. The lesions are pink to red macules and papules, and they may become confluent on the body Most of the rash has faded within forty-eight hours There is generalized adenopathy most marked in the posterior triangle of the neck

ROSEOLA (sixth disease pseudo-rubella)

This is a mild disease of young children with an incubation period of 7 to 17 days After 3 to 5 days of malaise and fever (high enough to give convulsions in infants) a fine macular or maculo-papular rash appears on the trunk and spreads to the limbs and face General signs disappear as the rash comes out and the rash soon fades.

INFECTIOUS MONONUCLEOSIS (glandular fever)

After an incubation period of 4 to 14 days the disease begins gradually or abruptly with malaise fatigue and irritability Then follow fever chills and sweating nausea and vomiting and headache There is generalized adenopathy marked in the neck, and the spleen may be a little enlarged There is sore throat even ulceration in adults Many patients have a morbilliform or rubelliform rash this is commonest when the glands are least affected Erythema nodosum is occasionally encountered Hepatitis occurs in some epidemics

infection rarely suffers again in after life Generally a child developing many lesions will be cured before one with only a few Adults rarely develop the enormous crops of warts sometimes seen in children and they have much less tendency to spontaneous cure.

Histopathology The basic histological feature of regular hypertrophy of the strata corneum, granulosum and Malpighii is seen in all types and in most cases there are large vacuolated cells in the stratum granulosum and upper layers of the stratum Malpighii There are varying degrees of change in the different types and alternating areas of hyper and parakeratosis are seen in verruca vulgaris and verruca plantaris. Papillomatosis is marked except in verruca plana. Long thin dermal papillae run up high into the epidermis and show when the wart is trimmed, as bleeding points or as little black points when thrombosed as they often are in warts on pressure points such as the palms or soles.

Plane or flat warts (*verrucae planae*) occur usually on the face, the dorsa of the hands and forearms or legs in children. The



FIG. 89
Plane warts.
University of Pretoria

lesions are generally numbered in many hundreds and are small, flat, yellowish-brown papules, 1 to 5 mm. in diameter

infection are *epidemic pleurodynia (Bornholm disease)*, aseptic meningitis and some non-specific febrile disorders.

Herpangina is a common disease of children or young adults, most cases occurring in children between 1 and 7 years old It occurs oftenest in small epidemics but sporadic cases may be encountered After an incubation period of about four days the disease begins with high fever and sore throat. *Vomiting is common, convulsions may occur in children* and anorexia and prostration may be marked Lesions appear on the mucosa of the fauces tonsils, pharynx soft palate and occasionally elsewhere in the mouth or on the tongue The lesions are greyish white pinhead-size papulo-vesicles surrounded by a bright red areola. *Ulceration follows* but healing is usually complete within a week In one case in a young adult recently *seen herpangina followed immediately on* an attack of Bornholm disease

Aphthous, acute herpetic gingivo-stomatitis measles and chickenpox may have to be considered in differential diagnosis.

Treatment is purely symptomatic.

WARTS

The four varieties of warts (verrucae) of skin and mucous membranes are all caused by identical or allied strains of a virus. The clinical type is conditioned by the area of skin infected e g *condylomata acuminata are seen on moist areas* such as the genitalia plane warts occur usually on the face or dorsa of the hands Warts are contagious and many successful experiments in passage have been reported but although virus like particles have been seen with the electron microscope it has not yet been possible to culture the virus

Warts are species-specific and it is not possible to inoculate *animals with human warts and vice versa It seems* certain that most people develop an immunity against the infection some possibly as a result of latent infection warts are so common that it seems unlikely that anyone could escape contagion yet many people never develop them Most infections occur in children and when warts *are seen in an adult it is usually* found that the patient escaped attack in early life A child having a gross



FIG. 90
Common warts.



FIG. 91
Subungual wart. Mosaic plantar warts.

that usually stay discrete but may coalesce to plaques (Fig 189). A Koebner like phenomenon of a row of lesions along a scratch mark is often seen. Lichen planus may be closely simulated, but the distribution is different.

A rare condition which may be a variant of plane warts is *epidermodysplasia verruciformis*. The disease usually begins in childhood and shows no tendency to spontaneous cure. The lesions are like those of plane warts in all respects and affect mainly the uncovered skin often forming plaques. Inoculation experiments have been successful suggesting that the disease is infective but some authorities still believe that it is a naevoid disorder and allied to *acrokeratosis verruciformis* where similar warty lesions and plaques are seen on the dorsa of the hands and feet. A striking feature of epidermodysplasia verruciformis is that there is a marked tendency for squamous carcinoma to develop in the lesions this is an extremely rare but by no means unknown occurrence in ordinary warts.

Filiform warts are fine thread or tag like lesions seen oftenest about the face corners of the mouth neck, axillae and groins. They are common on the beard area in young men and are probably spread by shaving.

Common warts (verrucae vulgares) are dome-shaped or cauliflower like papules or nodules occurring mainly on the uncovered skin in children especially on the hands arms and knees (Fig 190). There are almost invariably multiple lesions. Sometimes in children one sees several varieties of warts on one patient. The scalp is frequently affected in adults perhaps from infection at the barber's shop. Sub- and periungual warts may be most painful and disabling.

Plantar warts (verrucae plantares) are seen as callus like thickenings on the soles usually at pressure points (Fig 191). They are distinguished from calluses by being more painful and by having tiny black dots (thrombosed dermal capillaries) in their surface shaving of the superficial hyperkeratosis may be necessary to demonstrate this. Similar lesions may be found on the palms in manual workers. A special variety is the mosaic wart where many lesions have become aggregated to a large pitted plaque. Multiple discrete or mosaic lesions, sometimes with enormous hyperkeratosis covering the whole sole may occur and are not infrequently seen in the Bantu of South

Africa. Common warts on the toes and elsewhere often go with plantar warts in children

Moist warts (condylomata acuminata) are exuberant, red (or white on mucous surfaces) moist and fleshy papules or papillomatous growths. They are often seen on the genitals (glans, prepuce urethral orifice in both sexes, labia, vagina) the perianal region and even into the anus and on the buccal and ocular mucosa (Figs. 192 and 193) Malignant change, though very rare in warts, usually occurs in this variety (Fig 194)



Fig. 94

Condylomata acuminata of anus. Squamous-cell carcinoma arising on warts

(Department of [illegible] University of Pretoria

Treatment The vast majority of warts disappear spontaneously within a few months to two years, though some, especially in adults, seem to persist indefinitely This is doubtless the reason why suggestion works so well in some cases. It is noticeable, however that the statistics on cures by suggestion seldom list any convincing claims of good results in plantar warts which are notoriously harder to cure than any others.

Into the same category as suggestion and psychotherapy fall the systemic treatments with such drugs as arsenic, bismuth vitamins, antibiotics and antihistaminics to mention only a few No effective vaccine has yet been prepared

In the case of multiple common warts in children by *far the best* plan is to reassure the parents that they will disappear



Fig. 192
Condylomata acuminata.

[illegible]

Fig. 193
Condylomata acuminata

Subungual warts present a very difficult problem because of their inaccessibility and if chemicals (see under plantar warts) fail it may be necessary to anaesthetize the patient and make a clean sweep with diathermy Like plantar warts they often show little tendency to spontaneous cure, especially in adults.

Plantar warts are the most difficult of all to cure. About 25 per cent disappear spontaneously within a year but they may cause so much pain and discomfort in walking that few patients will be consoled by this faint hope. In the first instance occlusion with Elastoplast should be tried and the patient should attend weekly for scraping and cleaning of the wart before replastering The plaster must be of 3-inch material and applied around the foot to support the arch and relieve pressure small patches are quite useless. This treatment may be modified by applying a keratolytic ointment of 25 per cent salicylic acid to the wart, surrounded by a carefully cut and pared felt ring Other chemicals such as phenol or nitric acid can also be applied after the lesion is cleaned at the weekly visit.

Another simple treatment is the twice daily application of 10 per cent formalin solution. The solution can be put in a plate and the patient sits with the affected part of the sole in the solution for 10 to 30 minutes twice daily The effect is to desiccate and harden the tissues which can be pared off at weekly intervals. If the surrounding skin is being damaged by this method of application the patient can use a plug of cotton wool or a medicine bottle with a neck of appropriate size to apply the solution more precisely to the wart. Formalin is also worth trying, applied on cotton wool, for subungual warts.

If simple measures fail, and they must be tried for a reason ble period of at least six weeks, the wart may be curetted out under local or general anaesthesia and the raw base treated with diathermy

Mosaic plantar warts should be pared off and then have trichloracetic acid rubbed in, followed by rubbing with a silver nitrate stick. Elastoplast is applied round the foot and treatment is repeated once a week. Of all the plantar warts these are the most stubborn.

When orthopaedic defects coincide as they often do, they must be corrected if good results are to be expected

in time and to prescribe some innocuous remedy as a placebo if necessary

Surgical excision of warts is not recommended as the risk of recurrence in the scar is high Common and filiform warts if few in number can be easily removed with diathermy local anaesthesia is not necessary for the smallest lesions. A similar effect can be produced with carbon dioxide snow applied firmly for 1 to 3 minutes if treatment is successful a blister forms and lifts the wart which can then be snipped off

Chemical destruction is often used, especially in younger children who are likely to resent local anaesthesia Salicylic acid may be applied as an ointment (25 per cent) and strapped on or specially prepared plasters may be obtained. It may also be applied in collodion (25 per cent) When strong caustics such as liquid phenol trichloracetic acid or nitric acid are used care should be taken to protect adjacent skin by ringing lesions with Vaseline Phenol followed by nitric acid is recommended by some Before using caustics any hyperkeratotic surface material should be pared off

Occlusion of warts with Elastoplast is possible in some situations and is simple and relatively effective The plaster is left on as long as possible and when it is removed the softened wart tissue is scraped off before a new plaster is applied Treatment may take 4 to 6 weeks

Podophyllum resin 25 per cent in alcohol or liquid paraffin, may be extremely effective in cases of *condylomata acuminata* especially of the genital and anal regions The liquid must be applied precisely to the warts with the surrounding skin protected by Vaseline as a violent reaction may occur and cause great oedema if it spreads After treatment the patient lies quietly for five minutes and then all redundant liquid is removed and the area liberally powdered Treatment may have to be repeated after a week or when all inflammation has subsided Podophyllum has also been used in the treatment of skin carcinomas and papillomas of the bladder It has little or no effect on any warts apart from the moist variety

Plane warts on the face should always be cautiously treated for fear of leaving scars If spontaneous cure is too long delayed they may be touched with trichloracetic acid or sparked with the diathermy

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When orthopaedic defects coincide, as they often do, they must be corrected if good results are to be expected.

Radium and x ray therapy are used only in desperation Even in the most competent hands there is some danger of severe necrosis resulting in chronic ulcers that often require plastic repair

MOLLUSCUM CONTAGIOSUM

This viral disease affects the skin and occasionally the conjunctiva. The individual lesion is a discrete shiny white



Fig 193
Mollusca contagiosa.

yellow or pink domed papule which as it develops, becomes centrally umbilicated (Fig 195) When they appear the papules are 1 to 2 mm in diameter and the fully developed lesions are usually 5 to 10 mm but much larger giant mollusca" are sometimes seen Any part of the surface except the palms and soles may be affected and there are almost always multiple

lesions, sometimes in a localized area such as the face, chest or genital region, sometimes widely disseminated. When a lesion is squeezed it extrudes a gritty white central mass. Occasionally in cases with only a few localized lesions there occurs a sudden wide dissemination that suggests a viraemia.

Molluscum contagiosum is not a very common disease, but experiments in passage suggest that many people may have had inapparent infections and so developed immunity. The mode of spread is not always obvious as many patients can give no history of contact with affected people. Sometimes, however, it seems to be spread by venereal contact or by masseurs, etc.

Histopathology. The epidermis grows down in multiple lobules into the dermis. Many epidermal cells undergo a particular form of degeneration as they advance from the basal layer towards the surface, where desquamation leads to the formation of the central depression in the papule. Large cytoplasmic inclusion bodies form in the epithelial cells and enlarge until they exceed the size of the original cell whose nucleus remains only as a crescent at the periphery. The virus is easily distinguished in the cells by electron microscopy.

Treatment. Spontaneous disappearance of all lesions is rare and the condition may persist for many years. Individual lesions regress as the result of trauma or secondary coccal infection. The lesions can easily be removed by curetting, diathermy or the application of a little liquid phenol on a sharp toothpick driven into the central core. Anaesthesia may be required if the lids and adjoining conjunctiva are affected.

Antibiotics such as aureomycin, locally or systemically are not reliable, but I have had a few successes with oral treatment in cases where there was a sudden dissemination of the lesions. There is no point in trying them if only a few lesions are present.

MILKER'S NODULES

The commonly-occurring cowpox of the present day is distinct from the Jennerian cowpox of earlier times (now rare) and from vaccinia. When man is infected, inflammatory lesions known as milker's nodules are seen. The condition in man is

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[St John

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Recently an epizootic pseudo-aphthous stomatitis of cattle has been described infection in man causes lymphocytic meningitis and, usually an exanthem. In two cases patients had previously suffered from milker's nodules, suggesting a relationship between the two diseases.

In differential diagnosis must be considered the various conditions to which milkers are liable, cowpox, foreign body granuloma (cow hair) callosities (tylositas symetrica hallucis of Tryb) verrucous tuberculosis and warts, granuloma pyogenicum, boils and impetigo

The virus of milker's nodules has no immunological relationship to those of the cowpox-vaccinia group and Jennerian vaccination offers no protection against milker's nodules. Electron microscopy also demonstrates that different viruses are involved.

Histopathology There is marked hyper and parakeratosis and acanthosis with digitate projections of epidermis deep into the dermis which shows a dense round cell infiltrate and many newly formed capillaries. There is oedema of the epidermis and sometimes a shallow sub-corneal bulla containing leukocytes.

Treatment is usually unnecessary as the lesions heal spontaneously Antibiotics have no apparent effect on the speed of healing but may be necessary if there is secondary infection.

ORF

Orf, otherwise known as ecthyma contagiosum or ovine contagious pustular dermatitis, is a disease of sheep and goats which is occasionally transmitted to man. The lesions in animals are found on the hairless skin of the nose lips, eyelids, teats and ano-genital area and in the mouth macular at first, they become in turn papular vesicular pustular and finally papillomatous and crusted.

probably far commoner than is suggested by the relatively sparse literature because the lesions are unimportant, spontaneously healing and probably considered to be boils or some such banal condition

In cattle the disease produces pustular and crusted lesions of the teats and udders known as natural false or pseudo-cowpox or para vaccinia Lesions in man appear about a week



Fig. 96
Milker nodule with follicular keratotic side reaction

after handling an infected animal on the hands or fingers, more rarely on the arms face or neck There are rarely more than one or two A fully developed lesion is a tense shiny dark red or purple domed or conical nodule 5 to 20 mm in diameter (Fig 196) The top is flat or slightly umbilicated and covered with a greyish epithelium When this is removed a moist granulating surface is seen There is no tendency to frank vesicle or pustule formation or to haemorrhage Healing usually without scar takes place in 4 to 6 weeks Local inflammatory oedema lymphangitis and regional adenopathy may be noted and secondary coccal infection whitlow etc may

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Lesions in man appear between 4 and 7 days after direct or indirect contamination by an infected animal on the exposed skin of the hands arms or less often the face The lesions, of which there may be one or several and which bear a notable resemblance to those of milker s nodules, go through macular papular vesicular (possibly haemorrhagic) and crusted phases to heal in about a month (Fig 197) Constitutional symptoms are absent or in conspicuous but there may be a mild regional lymphadenopathy or local secondary coccal infection

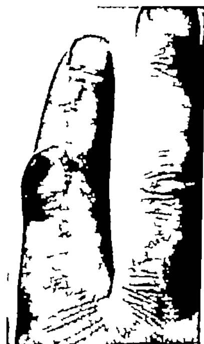


FIG. 97
Orf
(G. A. Grant Peterkin British Journal of Dermatology)

Histopathology The histological picture though not specific, is suggestive of a viral infection with hyperkeratosis, parakeratosis, acanthosis, intra epidermal vesicles, reticular degeneration of epidermal cells and an acute inflammatory dermal infiltrate

The problems in differential diagnosis are the same as those in milker s nodules and the only major difference between orf and milker s nodules is that the one is contracted from sheep or goats, the other from cattle It has been postulated that the two diseases may in fact, be identical but the orf of sheep cannot, apparently be experimentally transmitted to cattle.

Treatment other than symptomatic is unnecessary

CAT SCRATCH DISEASE

The primary lesion which usually but not invariably follows 3 to 14 days after a cat scratch or bite is an inflamed area sometimes with papule formation or even central necrosis.

One to three weeks later the regional glands become markedly enlarged inflamed and tender and may go on to suppurate and discharge through the skin. There is malaise fever headache and sometimes generalised adenopathy and splenomegaly A maculo-papular or papular rash of the body and limbs is often seen and erythema multiforme has occurred in a few cases. Encephalitis has been reported General symptoms subside in a few days to a week or two but the glands may take months to return to normal.

A few cases are described where the disease began with unilateral conjunctivitis and enlargement of the pre-auricular lymph gland and infection may also take place from the naso-pharynx.

The causal agent is believed to belong to the psittacosis-lymphogranuloma group Inoculation of pus from a lymph gland into the skin will produce in an infected person, after forty-eight hours, a papule with central necrosis and wide surrounding erythema. A small number of people who keep cats are said to give a positive reaction.

Treatment with aureomycin or terramycin may be given but the true value of antibiotics has not yet been assessed

LYMPHOGRANULOMA VENEREUM
(L. inguinale, Nicolas-Favre disease)

This venereal disease caused by one of the chlamydozoaceae, produces lesions commonly localized to the inguinal, genital and pelvic regions and occasionally systemic manifestations.

After an incubation period of 3 to 21 days a small vesiculo-erosive or papular lesion appears on or about the genitals or exceptionally on extragenital areas. This primary lesion is often concealed or fleeting and unrecognized. A week or two later the regional glands, usually inguinal, sometimes pelvic in women, become enlarged (buboes) and often go on to suppuration and abscess and fistula formation (Fig 198) In the early stages there is fever malaise, headache and loss of weight.

The inguinal glands on one or both sides may be affected. In some cases they subside without suppuration, but usually

Lesions in man appear between 4 and 7 days after direct or indirect contamination by an infected animal on the exposed skin of the hands arms or less often the face. The lesions, of which there may be one or several and which bear a notable resemblance to those of milker's nodules go through macular papular vesicular (possibly haemorrhagic) and crusted phases to heal in about a month (Fig 197) Constitutional symptoms are absent or inconspicuous but there may be a mild regional lymphadenopathy or local secondary coccal infection



Fig. 197

Orf

[G A Grant Peterkin British Journal of Dermatology]

Histopathology The histological picture though not specific, is suggestive of a viral infection with hyperkeratosis, parakeratosis, acanthosis intra epidermal vesicles, reticular degeneration of epidermal cells and an acute inflammatory dermal infiltrate

The problems in differential diagnosis are the same as those in milker's nodules and the only major difference between orf and milker's nodules is that the one is contracted from sheep or goats, the other from cattle It has been postulated that the two diseases may in fact be identical but the orf of sheep cannot apparently be experimentally transmitted to cattle

Treatment other than symptomatic is unnecessary

CAT SCRATCH DISEASE

The primary lesion which usually but not invariably follows 3 to 14 days after a cat scratch or bite is an inflamed area sometimes with papule formation or even central necrosis

The commonest of the systemic manifestations are skin eruptions, presumably as a result of viraemia in sensitized subjects. Scarlatiniform and other similar erythemas and erythema nodosum may occur Rashes on exposed skin (lucites) are not uncommon. Generalized adenopathy splenomegaly arthritis, meningo-encephalitis, bronchitis and pneumonitis have been found in rare severe cases.

In some cases the disease occurs in the eye giving a severe acute conjunctivitis and sometimes keratitis and iritis



FIG. 99
Lymphogranuloma venereum. *Enlarged*
(C. K. O'Malley

Lymphatic obstruction may cause gross oedema of the lids. Marked corneal damage may occur

Cutaneous sensitivity can be demonstrated in infected people by Frei s test. Frei originally used pus from buboes, but infected chick yolk sac (Lygranum) is now employed. 0 1 ml. is injected intradermally and a positive reaction appears in forty-eight hours as an indurated papule at least 6 mm. in diameter with surrounding erythema. Except in cases treated very early and energetically the test will remain positive throughout life. For this reason reinfection is extremely rare

Treatment. Sulphathiazole, sulphadiazine, aureomycin and terramycin are the most effective remedies penicillin and streptomycin have little effect except on secondary infection.

the glands soften and multiple multilocular abscesses and discharging fistulae are formed and these, in the absence of treatment may take months or even years to heal. Inguinal lesions are commoner in men than in women



Fig 198

Lymphogranuloma venereum.

[Neil L. Murray]

The lymphatics of the penis are sometimes affected and this leads to multiple small abscesses and later ulceration. This, with inguinal glandular lesions, may lead after months or years to elephantiasis of the genitals. The vulva and vagina may be similarly affected. Polypoid growths of the anal region are also seen especially in women.

As a result of pelvic lymphatic glandular involvement in women (rarely in men) there may follow an inflammatory stricture affecting 3 to 10 cm of the rectum. Symptoms may resemble those of ulcerative colitis or there may only be increasing constipation. Stricture may occur alone or with ano-genital lesions. The tissues of the buttocks, perineum and thighs may become riddled with abscesses and fistulae (Fig 199). This state is known as *esthiomène*, it may be caused by other infections such as tuberculosis.

The male urethra is occasionally involved with infiltrative lesions and later stricture of the posterior part.

It is possible that some cases of *Peyronie's disease* induratio penis plastica are due to lymphogranuloma venereum. In this condition there is a woody induration of bullet shaped areas of the corpora cavernosa causing the penis, in erection, to deviate to one side or the other. The skin is not affected. It is extremely resistant to treatment.

diseases of this group which are found in various parts of the world.

South African tick-bite fever It is probable that all the tick transmitted rickettsial diseases of Africa are the same disease with different vectors. In South Africa the *R conorii* (*var pijperi*) is transmitted by most species of ixodid ticks and the organism is harboured in nature by various species of veld rodents.

The disease has a characteristic picture and begins after an incubation period of 5 to 18 days with chills, fever severe headache and generalized pains. The site of the tick bite is usually obvious as a black eschar surrounded by erythema and the regional lymph glands are enlarged In cases of primary infection through the eye there is severe conjunctivitis. A generalized maculo-papular erythematous rash, spreading as far as the face palms and soles, appears on the second or third day red macules may be seen on the palate (Fig 200) The central nervous system may be involved with delirium, irritability difficulty in micturition etc

Treatment Aureomycin 1 g followed by 250 mg six-hourly causes dramatic improvement after about forty-eight hours, but treatment should continue for three days after the fever has subsided.

It is not clear whether patients are cured by these drugs or whether a carrier state persists

RICKETTSIAL DISEASES

The epidemic diseases of the typhus group do not fall within the scope of this book and only the South African variety of tick typhus will be described as an example of the



FIG. 200

South African tick bite fever

Top. Primary sore or eschar which develops at site of attachment of infected tick. *Bottom.* Rash of tick bite fever in patient with primary affection of right eye

J. H. [illegible] *Museum of Medical* [illegible]

diseases of this group which are found in various parts of the world.

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CHAPTER XVI

FUNGOUS INFECTIONS

FUNGI are extremely widespread in nature and occur as saprophytes and parasites of man animals and plants only a very few of the great number of species are parasitic in man. Only two species of the genus pityrosporum *P ovale* and *P orbiculare* are saprophytic on the human skin

Certain parasitic fungi affect only the skin surface others affect the skin and sometimes other organs and yet other fungi have a predilection for the deeper tissues and organs and affect the skin only occasionally and as a minor phenomenon in the disease process The vast majority of fungous infections in man are of the first type.

The skin is protected to some extent against fungous infections by fungistatic substances present in the sebum The fungistatic properties of sebum are demonstrably important in ringworm infections of the scalp the adult scalp is only exceptionally infected by the fungi that commonly cause ringworm in children and seldom by others and intractable tinea capitis in children usually disappears spontaneously at puberty when the sebaceous glands adopt their adult function Areas of skin devoid of sebaceous glands, the palms and soles, are especially liable to infection by the common dermatophytes. Variations of distribution of fungistatic substances from one individual to another may play some part in the varying liability to common infections such as tinea pedis

Recent experiments on cultured skin suggest that the localization of ringworm infections to the dead keratinized structures in a living host may be the result of a fungistatic action of blood serum When serum factors are absent mycelia readily penetrate all the layers and structures of the skin

The superficial mycoses are caused by parasites which live on and in the stratum corneum seldom actively invading the deeper living layers of the epidermis Two main groups of

fungi are involved the ringworm group which is capable of keratinolysis and another group which does not possess this property

The ringworm fungi dermatophytes, can digest the formed keratin of the epidermis, nails and hair but they rarely penetrate except accidentally the formative cells of these structures. Three genera are involved trichophyton epidermophyton and microsporum and their species are of worldwide distribution. Some species are preferentially parasitic on man, others commonly attack animals but may be communicated to man.

Although the dermatophytes live only in the dead keratin they cause a variable degree of inflammation in the underlying tissue, presumably as a result of an allergic response to and perhaps irritation by products of the fungus The development of local immunity would explain the central healing and spreading ringed appearance of the lesions seen in classical ringworm. The rings do not spread indefinitely and there is a general tendency to spontaneous cure the speed of resolution being in proportion to the degree of inflammatory reaction. Inflammation is minimal in those chronic fungous infections where central healing does not occur or where recurrence takes place in once-healed areas.

Generalized hypersensitivity frequently develops, especially with severe inflammatory infections, and reactions in skin remote from the focus of infection, dermatophytides, are common. They result from the passage of fungous elements, or perhaps their allergenic products, into the blood stream and their dissemination. Fungous elements have on occasion, been cultured from the blood and found in the ide lesions in such cases. The allergic state may be demonstrated by the intradermal injection of trichophytin (prepared usually from *T mentagrophytes*) an immediate urticarial reaction may appear within half an hour but a papular reaction after forty-eight hours is more trustworthy The same antigen may be used for all the dermatophytes as they cross-react. The trichophytin test has little practical application.

The ringworm fungi are demonstrable by direct microscopy but they can be precisely identified only when cultured. Rough identification is possible by microscopic examination of

hair which is attacked by microspora and trichophyta, but never by epidermophyta *Microspora produce small spores* visible around the hair (small spore ectothrix) Trichophyta grow either entirely within the hair (endothrix) or produce external spores (large spore ectothrix) larger than those of the microspora

Specimens for microscopic examination are mounted in 10 to 20 per cent potassium hydroxide on a slide under a cover slip Skin scrapings from the edges of lesions or the tops snipped from bullae become translucent after about fifteen minutes and fungous elements become identifiable gentle warming hastens the process The beginner must guard against mistaking for fungous hyphae bubbles foreign bodies and mosaic fungus an artefact which appears as a dotted line between the epithelial cells Nail specimens should be taken from the subungual hyperkeratotic material and allowed to soften for a few hours or even overnight until they can be squashed flat under the cover slip Hairs should be plucked from active lesions and the use of Wood s light helps in many cases when fluorescent hairs may be chosen

The hyphae of all the ringworm fungi look the same in hair and nails When precise identification is necessary cultures must be made Specimens of skin nail or hair are sent to the laboratory either in a dry bottle or between two microscope slides the time spent in transit is immaterial and a few days should always elapse before planting cultures to allow bacteria to die off As the clinical appearances are generally sufficient to indicate the line of treatment cultures are made only in special instances which will be indicated or for the purpose of epidemiological study

Biopsy is rarely required in the study of the ringworms, but fungi may be demonstrated in sections stained by the Hotchkiss-McManus technique which may also be used on skin scrapings

Examination under Wood s light (ultraviolet rays passed through nickel-oxide glass) is a useful aid to diagnosis and guide to progress in tinea capitis In the case of the common microsporum infections infected hairs fluoresce a bright clear green Absence of fluorescence is no guarantee that fungous infection is absent because some trichophyton species (e g *T*

mentagrophytes *T* *ferrugineum* and *T* *rubrum*) cause no reaction and fluorescence is often slight with other trichophyta The presence of ointments invalidates the test. A yellowish-brown fluorescence of the scales is seen in tinea versicolor and Wood's light may be used here as a rough test of cure

No attempt will be made to list all the species of dermatophytes that have been identified as causes of ringworm, but the habits of the main genera and species are as follows.

Microsporum infections (especially *M* *audouini* and *M* *canis*) are the commonest causes of tinea capitis in most parts of the world. The skin and, rarely the nails may also be infected by microspora.

Epidermophyton floccosum is a common cause of tinea pedis and tinea cruris it may affect nails, but never hair

Endothrix species of trichophyton (e g *T* *schoenleini* and *T* *violaceum*) attack hair skin and nails ectothrix species (e.g *T* *mentagrophytes* and *T* *rubrum*) attack skin and nails, but rarely the hair

The allergides (dermatophytides microsporides epidermophytides, trichophytides) which often develop in sensitized individuals may be localized or disseminated and take a variety of forms which seldom resemble the primary focus of infection Dermatophytides usually erupt during or after a period of acute inflammation in the primary lesion such rashes may appear after over-energetic treatment or after x ray epilation

The commonest dermatophytide is a vesicular or bullous, and eventually squamous or eczematous, rash on the hands and sometimes the feet with tinea pedis. With tinea capitis patches of little lichenoid follicular papules, like those seen in lichen scrofulosorum may appear anywhere on the face, trunk or proximal parts of the limbs. Rarer dermatophytides include an erysipelas-like eruption of the legs scarlatiniform, macular papular or vesicular generalized eruptions and erythema nodosum, erythema multiforme or erythema annulare gyratum. Thrombophlebitis migrans, urticaria and a variety of other eruptions have been thought at times to represent dermatophytides. Only symptomatic treatment is required for such reactions which disappear when the primary infection is cured or subsides.

The non-keratolytic fungi subsist apparently on the non-keratinous constituents of the stratum corneum and do not attack hair or nails They cause little inflammatory response and never produce sensitization or ide reactions. The diseases involved are piedra trichomycosis axillary tinea versicolor erythrasma and tinea nigra All are banal chronic conditions causing unimportant symptoms or none at all

The deep fungous infections produce granulomatous lesions in the skin and other organs Some cause sensitization which is demonstrable by intradermal testing with specific antigens. The fungi can often be identified by microscopic examination of discharges or of biopsy specimens without the necessity of culture

Treatment The fungous infections, whether superficial or deep are notoriously impervious to treatment and there were until recently few which consistently responded to any specific remedy An enormous range of substances has been employed but although many antifungous agents are effective *in vitro* few act *in vivo* The picture is now changing since the discovery of antifungous antibiotics and it is possible that their use may alter the whole concept of treatment

The duration of a *ringworm infection* is indirectly proportionate to the amount of inflammatory response that it arouses and is relatively little influenced by topical treatment because no satisfactory keratolytic and fungicidal agent has yet been developed Infections by zoophilic fungi are usually inflammatory and relatively short lived while anthropophilic fungi cause little reaction and are often chronic and sometimes completely intractable the fungi behaving as saprophytes rather than as parasites and living a restful and safe existence behind the keratin barrier

A great number of chemical agents have been used against the superficial mycoses The list includes heavy metals, of which mercury salts are the most important iodine sulphur compounds fatty acids quaternary ammonium compounds, benzoic and phenol derivatives dyes, quinones and quinolines.

It was predicted that the ideal fungicide would be one which administered internally would endow the cells destined to produce keratin with the power to resist fungi this power persisting as they became keratinized Griseofulvin (Grisovin,

Fulcin) a metabolic product of *Penicillium griseofulvum* Dierckx may be just such a fungicide Both clinical and experimental observations indicate that all the keratolytic ringworm fungi will prove susceptible to griseofulvin but that other fungous pathogens affecting man are unlikely to be affected. *T rubrum* infections of the skin and nails, which are at best ameliorated by standard methods, respond in a remarkably short time skin lesions often begin to improve within a few days of starting griseofulvin treatment and healthy looking nail appears after a few weeks Many other notably resistant types of infection of the skin hair and nails are equally responsive It is too soon to say whether the effects will be lasting in all cases.

Griseofulvin is administered orally and appears to cause few toxic reactions and none of importance in the dosage required to treat ringworm infections. In the concentration obtained in human tissues it is probably fungistatic rather than fungicidal Optimum dosage levels and duration of treatment have still to be established

At the time of writing I prescribe 1 g daily (0 25 g 4 times daily) for three weeks and then 0·5 g daily until the condition is clinically and bacteriologically cured Severe headache may occur early in treatment, but should be ignored because it disappears in a day or two. A transient flare of inflammation may be noted in the first few days. Erythematous and urticarial rashes and gastric disturbances are reported

Methods of treatment for ringworm infections hitherto accepted as standard are still given in detail because it is obviously pointless to use griseofulvin for conditions which heal rapidly in any event, and because there will doubtless be cases in which it will be ineffective There is no contraindication to the use of local remedies as adjuvants while griseofulvin is being used

In other days potassium iodide was the mainstay of treatment for the *deep mycoses* but today it has largely been abandoned except for sporotrichosis against which it is most effective Some other chemical compounds which have been used for deep mycoses are fatty-acids, ethyl vanillate sulphonamides and sulphones, quinolines and aromatic diamidines. The sulphonamides are active against anaerobic actinomycosis

(though not the treatment of election) and South American blastomycosis and diaminodiphenyl sulphone is the drug of choice for nocardiosis

The antibiotics, particularly the antifungous polyenes, have altered the prognosis in many deep mycotic diseases. Penicillin in prolonged heavy dosage is very effective in actinomycosis and some of the other antibacterial antibiotics are also active here Nystatin (Mycostatin) a tetraene produced by a strain of *Streptomyces noursei* is active against candida infections, moniliasis in particular

Encouraging results are reported in the chronic and sometimes fatal deep mycoses after the use of amphotericin B (Fungizone) a heptaene antibiotic derived from a species of streptomyces The conditions in which it is indicated are cryptococcosis, coccidioidomycosis histoplasmosis North American and South American blastomycosis and disseminated moniliasis Amphotericin B has some activity when administered orally but the parenteral route gives best results. The antibiotic in powder form, must be dissolved in 5 per cent dextrose solution and the calculated dose is given daily by slow intravenous infusion over about six hours The solution for infusion should contain 1 mg per 10 c c An initial daily dose of 0·25 mg amphotericin B per kilogram of body weight is recommended but the dose should be slowly increased towards the optimum of 1 mg per kilogram Not all patients will tolerate this level of dosage but good results are reported in the 0 5 to 0 75 mg per kilogram range The total length of treatment varies greatly but improvement may be noticed after 4 to 8 weeks and infusions may then be given on alternate days

Toxic effects of treatment are encountered in almost every case and fever and chills, diminishing in time are to be expected at the outset, but may be limited by the prophylactic use of antipyretics or antihistaminics Headache nausea and vomiting are early side effects and the dosage must be adjusted to avoid them Phlebitis may occur The levels of blood urea nitrogen and non protein nitrogen must be regularly checked and the non protein nitrogen should not be allowed to exceed 40 mg per 100 c c Treatment may have to be temporarily suspended or given on alternate days to this end

Amphotericin B has been given intramuscularly and intrathecally in some cases and is reported to act against chromoblastomycosis when injected into the lesions

NON KERATOLYTIC FUNGOUS INFECTIONS

PIEDRA

Piedra is a fungous infection of the scalp, beard or moustache hairs caused by *Piedraia hortai* (black piedra) or

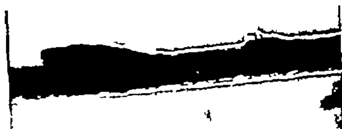


FIG. 201
Piedra due to *Piedraia hortai*

Trichosporon beigelii (white piedra) and occurring in tropical and temperate zones. Only the hair shaft is affected and little gritty nodules can be felt and seen on the hairs (Fig 201)

Treatment is with 5 per cent ammoniated mercury ointment or 1 per cent bichloride of mercury in 70 per cent alcohol

TRICHOMYCOSIS AXILLARIS

This disease affects only the axillary and sometimes the pubic hairs, producing irregular soft, nodular thickenings along the shaft. The nodules may be yellow red or black The cause of the basic yellow type may be a fungus, *Nocardia tenuis* or a corynebacterium. The association of cocci with the fungus produces the red and black varieties.

Treatment is as suggested for piedra the hair should be shaved.

TINEA VERSICOLOR (PITYRIASIS VERSICOLOR)

This common chronic disease of young adults in all climates is caused by *Malassezia furfur* The lesions are yellowish to light brown finely-scaling macules that often coalesce to form large plaques. Follicular papules may also be seen and there is a marked tendency for the disease to produce



FIG 202
Tinea versicolor

depigmentation which is most obvious on dark skins. Some people experience mild itch but generally there are no symptoms. The upper chest shoulders and back are usually involved, but much wider areas of the body and limbs may participate Lesions seldom spread further than the neck in the white races, but the face is often affected sometimes alone in the South African Bantu In Madagascar the disease when confined to the face and neck is known as *hodi potsy* (Figs. 202 and 203)

Tinea versicolor is distinguished from pityriasis rosea (short course) seborrhoeic dermatitis secondary syphilis and

fuligo by examination of scales which are always full of spores and mycelial elements. It is, in fact the disease *par excellence* for demonstrating fungi in epithelium.

Treatment If only small areas are involved 2 per cent sulphur and salicylic acid ointment is used. For large areas a saturated solution of sodium thiosulphate applied twice daily is more convenient. A simple treatment, which promises to be



FIG. 205
Tinea versicolor

effective, is by the application of Selsun lather for fifteen minutes every night for at least a month. Recurrence is to be expected if treatment is not thorough and continued for some weeks after lesions appear to have cleared Wood's light may be used to check progress. Depigmentation may take some months to be restored.

ERYTHRASMA

Erythrasma, caused by *Nocardia minutissima*, affects the groins, axillae and sometimes other skin folds. The distribution is like that of tinea cruris, but the pinkish to reddish-brown lesions, finely scaling, are quite flat and there is no vesiculation

in the spreading border Symptoms are negligible and the disease persists for years

Treatment is with the local remedies used for tinea cruris.

OTOMYCOSIS

Fungous infections may sometimes be the cause or probably oftener, contribute to the cause of a chronic or subacute dermatitis of the external auditory meatus and ear canal The commonest fungus found is *Aspergillus* The disease is encountered in warm climates and often starts after a holiday when the patient has been swimming a great deal. The epithelium becomes red oedematous and macerated and often itches a great deal Secondary impetiginization is common, as is dermatitis medicamentosa, for the disease is very resistant and patients usually try a great variety of applications.

Treatment The ear should be cleaned and cresatin or 2 per cent methyl green drops instilled Itch and bacterial infection often yield very satisfactorily to an antibiotic hydrocortisone lotion or ointment Prognosis must be guarded as this is one of the most stubborn conditions encountered in dermatology

TINEA NIGRA

Infection of the skin with *Cladosporium wernecki* produces black or brownish speckled macules that coalesce to form larger serpiginous plaques No scaling inflammation or vesiculation is seen The lesions are commonly found on the palms, the sides of the fingers or the wrists and very rarely elsewhere Fungous elements are seen in scrapings.

Treatment with any fungicidal ointment is rapidly curative

RINGWORM INFECTIONS

TINEA PEDIS

Tinea pedis athlete's foot is the commonest of all the dermatophytoses In most cases it is caused by trichophyta or epidermophyta very rarely by microspora or *Candida albicans* the clinical features in *Candida albicans* infections are clearly different from those of the common varieties. Children are

seldom affected and men suffer far oftener than women. Tinea pedis is a disease of shoe-wearers, and the barefooted are very seldom attacked except when they are working in hot damp conditions, as in mines, when the incidence rises a little. Hyperhidrosis and orthopaedic defects seem to predispose to



FIG. 204
Intertriginous tinea pedis.

infection. The disease has increased tremendously in incidence in the last fifty years, presumably because of the increasing use of communal swimming baths, changing-rooms and so forth.

The acquisition of tinea pedis and the form it takes are dependent, apart from the organism involved, on factors still

undetermined Some people are never infected, others have a single attack and thereafter remain free and yet others are constantly plagued Three major clinical forms occur but often one overlaps with the other

Intertriginous tinea pedis is the commonest variety and is usually the starting point for the other varieties. The lesions are seen between the toes and in the furrow under them. The



Fig. 203
Vesiculo-pustular tinea pedis.

cleft between the fourth and fifth toe is almost invariably affected and, indeed may be the only site of disease the larger cleft between the big toe and the second is often unaffected or suffers less than the others. There may be only superficial peeling of the epidermis or it may become soft white and sodden frank vesicles may be seen and splits may form in the depths of the clefts Spread to the under surface of the toes is common but the dorsal surface is rarely affected (Fig 204)

Symptoms may be negligible and many patients dismiss minor degrees of infection as simple maceration due to sloth in drying their feet but itching may be severe Intertriginous tinea pedis may last a season and disappear but often it

waxes in summer and wanes or clears in winter over many years.

Vesiculo-pustular tinea pedis commonly follows on the intertriginous, sometimes soon after the disease is first apparent, sometimes only after years of minor symptoms. The lesions are shotty and may be scattered sparsely or thickly over the sole or found in plaques, particularly in the hollow of the foot. There is a background of erythema and rupture of the vesicles leaves scaling (Fig 205). Large multilocular bullae may form. The dorsum of the foot and toes is rarely affected. This variety may be caused by actual infection, when fungous elements are recognizable in scrapings, or it may represent a dermatophytide reaction such as is seen on the hands: the difference is of no practical importance. This variety may clear up fairly rapidly or persist and fluctuate for very long periods.

Keratotic tinea pedis may develop from either of the other forms or arise *de novo* with or without intertriginous lesions. Trichophyton infections are responsible for such cases and cause a particularly recalcitrant chronic infection. The lesions are erythemato-squamous, and vary in severity from fine scaling to thick psoriasiform keratosis (Fig 206). Patchy distribution at pressure areas may be seen but often the entire sole is affected and the process may extend a little upwards over the sides of the feet. When *T. rubrum* is involved the lesions may spread over the feet and even to the ankles and legs. Episodes of vesiculation may occur and deep painful fissures may develop.

Infection of the nails is often associated and provides a constant focus for reinfection of the skin. Trichophyta are usually involved in such cases. The nails become thickened, hard and yellowish and may be deformed. The skin immediately adjacent to the nails is not always affected. Infection of the toe-nails is so impervious to treatment that it should be disregarded and any treatment given should be directed towards the protection of the skin against reinfection rather than against the onychia itself.

Tinea pedis is in most cases a chronic or subacute disease that causes discomfort rather than distress, but acute episodes may occur especially with the vesiculo-pustular variety or as a primary phenomenon and cause incapacitation (Fig 207)



Fig. 206
Keratotic tinea pedis.



Fig. 207
Acute tinea pedis

Acute tinea pedis may be entirely a result of the fungous infection or follow on secondary coccal infection. The feet become red, painful, swollen and oedematous vesicles and bullae may develop on the soles or on the dorsal surfaces. Lymphangitis, cellulitis and enlargement or even suppuration of the inguinal glands may ensue.

Dermatophytides are frequently observed in cases of tinea pedis and are usually confined to the hands where they appear



FIG. 208
Vesicular and squamous dermatophytides with tinea pedis.

oftenest as recurrent vesiculo-squamous eruptions, symmetrically distributed, on the sides of the fingers and the palms. The vesicular phase may not be apparent and all that one may see is patchy scaling in distribution suggesting that vesicles originally were present (Fig 208) Eczematous rashes are also encountered, often as a result of overtreatment of the original eruption. These allergides are sometimes more troublesome and prominent than the primary infection on the feet which may indeed, be ignored by the patient, but must never be



FIG. 206
Keratotic tinea pedis.



F[illegible] 20[illegible]
Acu[illegible] tinea pedis.

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Vesicular and squamous dermatophytides with tinea pedis.

oftenest as recurrent vesiculo-squamous eruptions, symmetrically distributed, on the sides of the fingers and the palms. The vesicular phase may not be apparent and all that one may see is patchy scaling in distribution suggesting that vesicles originally were present (Fig 208) Eczematous rashes are also encountered, often as a result of overtreatment of the original eruption. These allergides are sometimes more troublesome and prominent than the primary infection on the feet which may indeed, be ignored by the patient, but must never be

missed by the physician. In any case of cheiropompholyx or eczema of the hands of obscure origin it is essential to examine the feet tinea pedis is one of the commonest causes for such eruptions on the hands A clear history of flare of the foot lesions followed by eruption on the hands is acceptable evidence of the relationship some sufferers from chronic recurrent tinea pedis use the state of their hands as a reasonably accurate barometer for assessing when their feet need treatment

Dermatophytides of other types and on areas other than the hands are rare with tinea pedis, but eczematous plaques, erythema multiforme, erythema nodosum and erysipelas-like reactions on the legs occur on rare occasions, usually with trichophyton infections.

These fungous allergides have to be distinguished from allergic reactions due to medicaments used in the treatment of the primary infection It should be remembered that coccal infections and even allergic contact dermatitis of the feet may be complicated by reactions at a distance often on the hands. Tinea pedis is so common that its existence alone does not imply that it is the cause of eczema of the hands nonetheless it should always be treated even when it appears to be coincidental

Differential diagnosis presents little difficulty when typical intertrigo is present and other lesions are confined to the soles. Contact dermatitis from socks or shoes usually spares the toe clefts and affects the dorsa and pressure points of the toes and feet. Coccal infections may cause intertrigo but the lesions tend to spread to the dorsa rather than to the soles of the feet. Great difficulty may arise with acrodermatitis continua and pustular psoriasis confined to the feet biopsy and tests for the isolation of fungi may help in the investigation Psoriasis and squamous late secondary and tertiary syphilides may produce a picture clinically indistinguishable from keratotic tinea pedis biopsy and serum tests will solve the problem

Treatment Rest is essential for all cases with acutely inflamed lesions When the feet are inflamed and oozing nothing more than potassium permanganate baths followed by a drying lotion such as Castellani s paint and dusting powder should be used Painful vesicles may be pricked Dressings are harmful keep the parts cool under a bed cradle Secondary

coccal infections of a serious order should be treated with tetracycline antibiotics.

In cases of intertriginous and vesiculo-pustular tinea pedis where the lesions are not too moist or after the subsidence of an acute attack, the best results are usually achieved with ointments. The older remedies containing mercury salts (Phytodermine ointment is the best choice among proprietary preparations) and Whitfield's ointment are generally more effective than the modern fatty acid preparations (e g Mycil, Desenex) The last-named are useful for patients intolerant of stronger remedies as they only exceptionally cause irritation or allergic reactions. Whitfield's ointment is used particularly where the skin is dry and keratotic Instruct the patient to rub the ointment well in between the toes, below the toes and on any affected area on the soles excess ointment must be wiped off and the foot then powdered with a fungicidal dusting powder Phytodermine powder is very satisfactory as are Desenex, Mycil and similar preparations some patients cannot abide the smell of the fatty acid powders.

Keratotic tinea pedis responds best, if it responds at all, to keratolytic ointments. Whitfield's ointment, standard or double strength, may be used.

Patients should be advised to apply ointment and powder twice daily until they are apparently cured and then to continue using powder each morning for a few weeks longer Those liable to reinfection will be well advised to apply a fungicidal powder to the feet every morning as a routine for all time

There are many fungicidal preparations (e g Dequadin, Teoquil) besides those mentioned here and there is no objection to experimentation in stubborn cases provided the patient and his physician are aware of the dangers of sensitization to such remedies.

Patients should be advised to wear socks and shoes or sandals that allow the feet to be kept cool and dry Socks, of whatever material the patient finds most comfortable, must be changed daily and shoes should be worn in rotation. There is no way of sterilizing shoes and this is, in any event, unimportant since the fungi causing tinea pedis are probably universally present.

Griseofulvin is not indicated for minor infections and when it is used local remedies should be applied as well It is unlikely that griseofulvin used in an attack, will alter the innate susceptibility of some people to fungous infections of the feet.

TINEA MANUUM

Dermatophytides on the hands are common complications of tinea pedis and are usually vesiculo-squamous or eczematous in character Their relationship to the foot condition is usually obvious Treatment with *strong fungicides is* unnecessary the fungous elements have been destroyed in the allergic reaction. If minor they are best left untreated and if of major importance, they should be treated simply and symptomatically with baths and soothing applications Hydrocortisone lotions or ointments may be necessary in some cases and very severe bullous eruptions may occasionally deserve systemic steroid hormone treatment.

Fungous infections of the hands are rare in comparison to those of the feet. They may produce vesiculo-squamous or eczematous eruptions or diffuse keratosis of the palms and fingers Trichophyta are usually implicated and infections by *T rubrum* are especially stubborn the lesions are erythemato-squamous and may spread to the dorsa of the hands and to the wrists and arms The nails are eventually affected in many chronic cases (Fig 209)

Search for fungous elements is indicated in any case of chronic eczema of the hands particularly when the palms are involved

Treatment is on the same lines as for tinea pedis. Even the most chronic infections with *T rubrum* respond rapidly to treatment with griseofulvin

TINEA CRURIS ET AXILLARIS

Ringworm of the groins (dhobie itch) is a common complaint that of the axillae is much rarer Men are affected much oftener than women children are rarely affected Epidermophyta and trichophyta are the causative organisms the latter usually causing the more chronic infections Infections of the feet are *usually associated and the feet must* always be inspected in such cases and treated simultaneously if need be



Fig. 209

Tinea manuum

E. floccosum infection *T. rubrum* infection.

(P. W. [illegible])

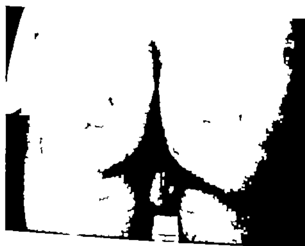


Fig.

Tinea cruris due to *T. rubrum* infection

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diagnosis must be established by demonstration of the fungus when only the axillae are involved

Treatment is on the same lines as for tinea pedis with rest, baths, lotions and powders in acute infections, ointments and powders for subacute and chronic cases. If tinea pedis is associated it must be treated as it may otherwise act as a reservoir of infection and lead to recurrences Griseofulvin should be used for stubborn cases, and from the start in trichophyton infections.

TINEA UNGUIUM

Ringworm of the nails is commonly caused by trichophyton (especially *T rubrum*) infections, less frequently by epidermophyton infections.

The toe-nails (one, several or all) are frequently infected in sufferers from tinea pedis and the infection persists after skin lesions have disappeared and frequently acts as a source of infection for recurrences on the skin Infections of the toe-nails cause no symptoms unless the nails are grossly deformed (and this is rare) because the immediately adjacent skin is seldom involved. The plates show varying degrees of thickening and there is crumbly subungual hyperkeratosis they are yellow in colour and often show a broad, irregular white band at the free edge that sometimes extends down the sides. They are usually very hard but may occasionally be friable (Fig 212)

Infections of the finger-nails are seldom ignored by the sufferer as are those of the toenails because the condition is not only unsightly but may also cause some discomfort. Some degree of infection of the skin of the fingers or hands is usually to be found. The infection starts in the lateral nail folds and invades th subungual keratin and the nail plate itself. At first there is simply yellow or white discoloration of the lateral edges of the nail but this slowly creeps over the plate which may remain hard or become soft and friable, breaking or crumbling off short. Subungual hyperkeratosis lifts the nail, sometimes so much as to loosen it or even cause it to be shed. It is the subungual keratin that should be scraped out for examination and not the nail itself which may be only sparsely infected especially on the upper surface.

Tinea cruris The lesions in the groins are usually bilateral and affect the fold of the groin and a semilunar area of the upper thigh the scrotum is seldom involved The onset may be acute when the skin is red swollen moist and vesiculated or macerated especially in the groin fold and at the advancing edge. Oftener the process is subacute and the affected skin is reddish brown and moderate scaling is evident at the active margins central healing may be apparent Sometimes spreading lesions reach as far as mid thigh and involve the lower abdomen and pubis, the perineum natal cleft and buttocks. (Fig 210) The perianal region may be the only site involved in some cases. Itch is an almost invariable complaint and may be intense.

To be considered in differential diagnosis are other fungous diseases such as erythrasma (very chronic, indolent lesions) and moniliasis (women oftener than men associated diabetes, pregnancy or obesity) psoriasis (especially in the elderly scrotum and penis often involved) and seborrhoeic dermatitis (pubis usually involved and evidence of disease elsewhere)



Fig. 211
Tinea cruris et axillaris
St John Hospital

Tinea axillaris may be unilateral or bilateral and is generally associated with tinea cruris (Fig 211) The lesions are of the same types as those seen in tinea cruris and involve the axillary fossa and may extend in circinate pattern downwards on the chest and arm In comparison with contact dermatitis and seborrhoeic or infective dermatitis, tinea axillaris is rare and the

enclosing a healing or inactive, often squamous, centre Spread continues for a few weeks and the lesion may finally reach 5 to 10 cm. diameter there it remains for a week or two before subsiding completely (Fig 213) There may be one several or rarely many lesions and confluence may produce gyrate



Fig. 213
Tinea circinata due to *M. canis* infection.

figures. Concentric rings are unusual in the common ringworms produced by microspora and *T. mentagrophytes* The diagnosis is usually obvious and in doubtful cases can be established by search for fungi in scales or tops of vesicles from the edge of a lesion conditions likely to be confused with tinea circinata are pityriasis rosea and streptococcal eczematides.

Almost any fungicidal preparation will hasten healing and mercurial ointments (e g Phytodermine) 2 per cent sulphur and salicylic acid ointment or a fatty acid ointment are satisfactory the use of iodine or dyestuffs is colourful, but unnecessary Griseofulvin may sometimes be necessary and is rapidly effective

Variants of tinea circinata are eczematous and vesicular lesions in which central healing is not so liable to occur These are probably missed oftener than they are diagnosed but since they heal spontaneously and quicker usually than the common ringworm, this is of little importance

A

Treatment Until the advent of griseofulvin any cures of onychomycosis were due oftener to chance than to intent. Avulsion and chemical destruction of the nail plates gave no better results than the hopeless application of iodine or ointments. Griseofulvin gives good results in *T rubrum* infections



Fig 212
Tinea unguium.

at least but treatment must continue till the nails are clinically and bacteriologically cured Infected nail should be cut, chipped or scraped away during the treatment period Asymptomatic infections of the toe nails need not be treated.

TINEA CORPORIS

Ringworm of the glabrous skin is caused by trichophyta and microspora and may take a wide variety of clinical forms The origin of the disease is often in some domestic animal and lesions in such cases are usually on the exposed skin

Tinea circinata from which ringworm takes its name begins as an erythematous papule but is usually seen when it has achieved its final form as a slowly enlarging ring with a raised, red vesiculated or scaling border 2 to 5 mm wide

erythema and vesicles and disseminated ide reactions may also occur (Fig 214)

Spontaneous healing occurs in from six weeks to several months. These trichophytoses usually respond rapidly to griseofulvin. Fomentations may be applied at first, a fatty acid ointment later

Granuloma trichophyticum (*Majocchi*) occurs usually in *T rubrum* infections and is oftenest seen on the legs. Women who shave their legs are reputed to be prone to this rather rare manifestation of trichophytosis. The lesions are little indolent, slightly elevated, dull red nodules with a smooth or scaly surface that may slowly disappear or necrose and heal with scarring They appear within an area affected by trichophytosis, or near such an area when the first sign is a little eczematous patch

The histological appearance is of a granuloma with foreign body giant cells about a fragment of hair in a disrupted follicle special staining demonstrates fungous elements.

Tinea imbricata (*tokelau*) is a variety of ringworm seen in the tropics. The lesions are large plaques composed of close concentric circles of flat papules and scales that overlap like shingles on a roof (Fig 215) Very large areas may be covered by the eruption which then produces bizarre whorled and gyrate patterns as plaques merge A brownish ring precedes the spreading edge of scales. Hair and nails are usually spared.



Fig. 215
Tinea imbricata.

Genuine tinea imbricata is caused by *T concentricum* infection Other trichophyta may produce concentric ringed lesions, but th rings are widely separated and the scales do not overlap

Erythemato-squamous plaques, slowly extending with gyrate borders, are due to trichophyton infections and the most stubborn are due to *T rubrum* Such plaques are commonly found on an arm or a leg having started at the extremity or on the buttocks or lower abdomen and groins The advancing edge shows most activity though vesicles are rare, and the central area may show a tendency to healing though it rarely clears up entirely Scaling is always present and marked hyperkeratosis is usually found when palms and soles are involved A whole limb may eventually be covered or large areas of the trunk recrudescence of activity in the inert central area may produce concentric rings which are almost always

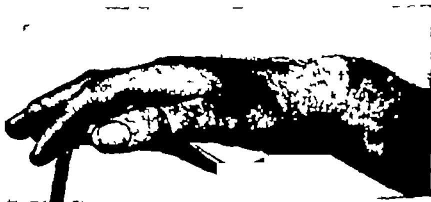


Fig 214
Tinea profunda.

quite distinctly separated one from another The inflammation is never severe though it waxes and wanes in intensity

The very chronic, dull red atrophic looking lesions are quite often mistaken for tuberculoid leprosy in lands where the two conditions occur examination of scales and biopsy settle this point

Griseofulvin should be used in cases of chronic trichophytosis Whitfield s ointment is usually the best local application

Tinea profunda is equivalent to kerion of the scalp and is generally seen in farmers and others who handle cattle The lesion is a soft circumscribed elevated granulomatous mass studded with pustules The surrounding skin may show

Spontaneous healing, sometimes with cicatricial atrophy occurs after several months. Griseofulvin promises to be effective. Fomentations should be used in the early stages and a fatty acid ointment later.

Sycosiform tinea barbae is relatively rare and clinically distinguishable from coccal sycosis barbae only if hairs are loose and being shed or breaking off short. Microscopic examination of hairs reveals the infecting fungi.

Fungicidal ointments and manual epilation of loose hairs may effect a cure, but griseofulvin will probably be the treatment of election in future.

TINEA CAPITIS

Ringworm of the scalp is caused by microsporum and trichophyton infections. It is by far the commonest cause of patchy loss of hair in children. The adult scalp is rarely attacked, except by some trichophyta, and persistent infections in children may be expected to clear up at puberty.

Boys are affected much oftener than girls, probably because their scalps are less well protected against access by spores and against trauma, which is apparently a necessary prelude to infection.

Microspora are the commonest causes in most countries. *M. canis* and *M. gypseum* infections are contracted from animals and seldom spread from child to child. *M. audouini* infections spread epidemically among children, but the percentage of the child population affected in an epidemic is never very high. The species commonly involved vary from one country to another e.g. *M. canis* infections are common and *M. audouini* infections are very uncommon in South Africa while in Britain *M. audouini* infections are commonest. *M. audouini* has never been isolated in Japan. *M. gypseum* infections are rare everywhere. The same variation is seen with the trichophyta and the rare fungous infection of today may be common in twenty years time.

A number of clinical pictures are seen in tinea capitis, but none of them can be related specifically to a certain type of infection. In localities where tinea capitis is not almost invariably due to a certain species of fungus it is wise to have the organism identified by culture as a guide to treatment.

Whitfield's ointment or 5 per cent sulphur and salicylic acid ointment are used in treatment, but the results are usually poor No reports have yet appeared on the use of griseofulvin in tinea imbricata but it is probable that it will have at least some effect.

Tinea barbae

Ringworm of the beard area in adults is caused by trichophyta and microspora and most cases occur in men working with cattle

Superficial circinate lesions identical with those of tinea corporis circinata and healing fairly quickly with simple



Fig. 216

Tinea barbae caused by an unidentified trichophyton.

treatment are sometimes seen but chronic *inflammatory* lesions are commoner

Granulomatous kerion like lesions are frequently encountered The area involved is often one cheek and the adjacent neck, but spread may involve the whole of the beard area and upper lip. The skin is swollen oedematous boggy and studded with pustules or covered with scabs (Fig 216) The hairs break off short or are shed they are loose and easily plucked out for examination. Fluorescence of hairs under *Wood's light* is found with microsporum infections

In some ringworms of the above type there is more evidence of inflammation and the scalp may be erythematous and show some superficial pustulation.

Major inflammatory lesions, *kerions*, may eventually develop on either of the above types or appear *de novo*. The affected scalp is elevated by a red boggy swelling covered with follicular pustules and the hairs are shed an abscess sometimes forms (Fig 218) Kerions heal within a few months, occasion-



Fig. 218

Kerions due to *M. canis* infection

ally with a certain amount of cicatricial change and permanent hair loss. They are caused by the fungous infection and not by secondary bacterial invasion (though this may occur) they cannot be reproduced artificially by the use of irritants on indolent lesions. Kerions may be caused by microspora or trichophyta.

Black dot ringworm, or *tinea tonsurans*, is caused by *T tonsurans* and *T violaceum* infections. Adults as well as children are susceptible and infections in children may persist into adult life The lesions are irregularly shaped, slowly spreading patches that show scaling but little or no erythema. A variable number of the hairs are broken off at scalp level the stumps showing as black dots, but many normal hairs are often left (Fig 219) Kerion is uncommon and the infection may and often does, persist for many years.

Id eruptions on the face and body are not uncommon with kerion and after x-ray epilation The rash is usually lichenoid

Only rough classification is possible as already noted, by microscopic examination of hairs and the use of Wood's light

The commonest scalp ringworm is characterized by spreading indolent ringed lesions which at first are comparable to those of the glabrous skin showing a slightly elevated papular or papulo-pustular edge and a scaly centre The rings



Fig. 217

Tinea capitis due to *M. canis* infection

grow to around 5 cm diameter and then remain static. In *M. audouini* infections the stratum corneum is by this time free but the infection persists in the growing hairs which may remain in this phase for some years before they are finally shed resting hairs are not attacked by fungi There may be one several or many rings which may merge and examination under Wood's light may disclose in cases of microsporum infection, odd infected hairs in parts not obviously affected Within the rings many hairs are lustreless and broken off short Microsporum infections are usually incriminated in such cases (Fig 217)

A little thought will make it obvious that the application of fungicides to the lesions of tinea capitis will, at best, have some effect on the unimportant infection of the stratum corneum and perhaps help to suppress the spread of infection the infected hairs must be shed spontaneously or be caused to be shed before cure is achieved. One fungicide is as good as another and Whitfield's ointment or 5 per cent ammoniated mercury ointment are commonly used, but it is probable that the result would be exactly the same if the ointment base alone were applied.

In boys the hair should be kept clipped short to facilitate treatment, but in girls of school age with only one or two discrete lesions it is unnecessary to insist on this. Skullcaps may be worn to keep the headgear from being soiled.

Kerions should be treated with potassium permanganate fomentations until the major swelling has subsided thereafter a fungicidal ointment is applied once or twice daily to the whole scalp. A daily shampoo is advisable at first, but twice weekly will suffice in the healing stage Major abscess formation and swelling of regional lymph glands implies secondary bacterial infection. Drainage and systemic tetracycline antibiotics may be indicated. Healing may not be complete for several months and regrowth of hair may not be obvious for as long as six months. X ray epilation of kerions is unnecessary and undesirable.

Spontaneous healing, assisted by daily application of fungicidal ointment, is to be expected in *M canis* ringworm and may occur in other types of infection where the lesions are obviously inflammatory even though short of kerion In *M canis* infections progress is checked by examination under Wood's light every 2 to 3 weeks until no fluorescent hairs remain It is essential that the child's head be shampooed and completely free of ointment for these checks.

Inflammatory *M audouini* infections may heal spontaneously but oftener they do not and the condition becomes stabilized and spreads no further after about three months. Treatment up to this point will have been as indicated above for *M canis* infections. When it is obvious that spontaneous healing will not take place x ray epilation must be arranged Epilation is frequently necessary for *T tonsurans* and *T*

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Differential diagnosis is seldom difficult in children where impetigo and psoriasis neither causing hair loss, are the only other common diseases of the scalp Alopecia areata is entirely



FIG. 219
Tinea tonsurans due t *T tonsurans* Infection.
John D Kn Ed

non inflammatory and exclamation mark hairs are usually to be found Because of its rarity in adults tinea capitis may long be missed unless broken hairs or stumps are noted and investigated

Treatment Spontaneous cure in 4 to 6 months may confidently be expected in *M canis* and *M gypseum* infections the rate of cure being proportionate to the degree of inflammation Kerions, whatever the cause may also be expected to heal fairly rapidly

Reasonably rapid spontaneous cure should not be anticipated in non inflammatory *M audouini* or trichophyton infections Factors other than the low grade of inflammation must be operative in this chronicity since *M canis* infections inflammatory or not are normally self healing

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depression in the scalp. The scutula are formed of fungus growing in profusion. A peculiar mousy odour may be present. The earliest stages of infection are seldom seen in the beginning

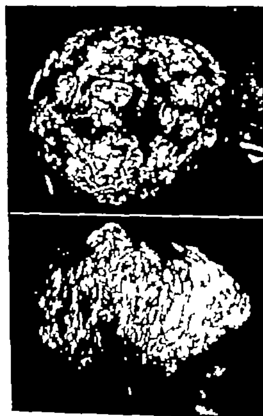


Fig 220

Favus.

(Courtesy of [illegible])

there are simply patches of erythema and scaling Later follicular pustules form and as they dry up the scutula take shape.

The scutula may remain discrete aggregate into larger plaques or be unrecognizable as a thick yellowish scaling reminiscent of seborrhoeic dermatitis or psoriasis (Fig 220) In

violaceum infections and may rarely be indicated in recalcitrant *M. canis* infections which do not, as expected, clear up after six months. The hair begins to fall about three weeks after an epilating dose of x rays and all the growing hairs will have fallen after about five weeks leaving only the resting hairs which are resistant and, in any case, uninfected. Regrowth begins about ten weeks after treatment. In the majority of cases epilation of the whole scalp is advisable. Opinion is divided as to the necessity for further local treatment after epilation in the case of microsporum infections, but it is essential in trichophyton infections. Epilation is almost invariably curative in microsporum ringworm, but the prognosis is not so certain with trichophyton infections.

An important question is whether or not a child with tinea capitis may attend school. My answer in *M. canis* infections is an unqualified affirmative and it is probable that the danger to other children is negligible with any type of infection, provided the sufferer is well-tended, anointed and capped. Any schoolmaster reasonable enough to accept pupils with ringworm is generally quickly made to change his mind by indignant parents.

Preliminary studies make it likely that the more elaborate procedures detailed above will seldom be necessary when griseofulvin is used. *M. canis* infections are apparently cured in about 6 weeks, *M. audouini* infections are reported to be equally sensitive and even the recalcitrant black dot ringworm due to *T. violaceum* responds well to treatment. The hair should be kept short and a fungicidal ointment used during griseofulvin treatment.

FAVUS (Tinea favosa)

Favus is a chronic ringworm infection commonly caused by *T. schoenleini*, but occasionally by *T. violaceum* or *M. gypseum*. Sporadic cases, often imported, are seen in civilized countries, but the disease is endemic in many backward areas all over the world. The scalp is usually affected but the glabrous skin and nails may suffer. Favus is usually contracted in childhood through contact with an infected person.

The characteristic lesions, known as *scutula*, are cup-shaped yellow crusts 2 to 10 mm. in diameter pierced by a hair or hairs. Removal of a crust shows a little red, moist or purulent

depression in the scalp. The scutula are formed of fungus growing in profusion. A peculiar mousy odour may be present. The earliest stages of infection are seldom seen in the beginning



FIG. 220

Favus.

(Courtesy of [illegible] Hospital)

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The scutula may remain discrete, aggregate into larger plaques or be unrecognizable as a thick yellowish scaling reminiscent of seborrhoeic dermatitis or psoriasis (Fig. 220). In

violaceum infections and may rarely be indicated in recalcitrant *M canis* infections which do not as expected clear up after six months The hair begins to fall about three weeks after an epilating dose of x rays and all the growing hairs will have fallen after about five weeks leaving only the resting hairs which are resistant and in any case uninfected Regrowth begins about ten weeks after treatment In the majority of cases epilation of the whole scalp is advisable. Opinion is divided as to the necessity for further local treatment after epilation in the case of microsporum infections, but it is essential in trichophyton infections Epilation is almost invariably curative in microsporum ringworm but the prognosis is not so certain with trichophyton infections

An important question is whether or not a child with tinea capitis may attend school My answer in *M canis* infections is an unqualified affirmative and it is probable that the danger to other children is negligible with any type of infection, provided the sufferer is well tended anointed and capped Any school master reasonable enough to accept pupils with ringworm is generally quickly made to change his mind by indignant parents.

Preliminary studies make it likely that the more elaborate procedures detailed above will seldom be necessary when griseofulvin is used *M canis* infections are apparently cured in about 6 weeks *M audouini* infections are reported to be equally sensitive and even the recalcitrant black dot ringworm due to *T violaceum* responds well to treatment. The hair should be kept short and a fungicidal ointment used during griseofulvin treatment

FAVUS (Tinea favosa)

Favus is a chronic ringworm infection commonly caused by *T schoenleini* but occasionally by *T violaceum* or *M gypseum* Sporadic cases, often imported are seen in civilized countries, but the disease is endemic in many backward areas all over the world The scalp is usually affected but the glabrous skin and nails may suffer Favus is usually contracted in childhood through contact with an infected person

The characteristic lesions known as *scutula* are cup-shaped yellow crusts 2 to 10 mm in diameter pierced by a hair or hairs. Removal of a crust shows a little red moist or purulent

In exceptional cases *T. schoenleini* has invaded the deeper layers of the skin, lymph glands and even the blood stream.

Favus shows little or no tendency to spontaneous cure at puberty or any other time and is contagious to adults.

The various causes of pseudo-pelade have to be considered in differential diagnosis. Diagnosis is made by examination of hairs and scutula and by culture. The fungus is seen in hair as chains of rather large rectangular cells (Fig. 221).

Treatment. Although favus of the glabrous skin may be controlled by local fungicides, onychia is usually incurable by such methods and infections of the scalp and hair are not always cured by x-ray epilation. The use of griseofulvin will probably end this unhappy state.

SYSTEMIC FUNGOUS INFECTIONS

MONILIASIS

Moniliasis or candidiasis is caused by species of candida, usually *C. albicans*, and is commonly manifested by superficial cutaneous or mucosal lesions and, more rarely, by septicaemia and visceral lesions. Pathogenic strains of candida are frequently saprophytic on the normal human skin, mucous membranes and bowel, so that their mere isolation is not evidence that they are causing any abnormality which may be present. Some change in the tissues of the host or in the ecological balance are usually necessary before the organisms become parasitic. Epidemics of moniliasis of various clinical types have, however, been reported and isolated passage of infection from one person to another is not rare.

Moniliasis is worldwide in distribution and may occur at any age in either sex. Buccal lesions are commonest in infants and in elderly people with chronic wasting diseases. Cutaneous lesions usually arise on macerated skin and malnutrition may be a predisposing factor. Diabetes and pregnancy predispose to vulvo-vaginitis. Endocarditis has been reported in drug addicts. The ecological balance of the intestinal flora may be upset by the modern antibiotics and their intensive use may be followed by superficial, and even fatal, systemic infections.

affected areas many of the hairs fall out, but odd tufts are left. The *hair is lustreless, atrophic and discoloured* and can be pulled out easily but it does not break off short as in other varieties of tinea capitis. Once hair has fallen it does not regrow and as the disease spreads peripherally the central *scutula fall off leaving an atrophic, scarred scalp*.



FIG. 221

T. schoenleini in scutulum of favus.

(F. P. S.)

Rarer forms of favus are impetigo-like, papyraceous with *fine papery scales* over a red ulcerated area, or alopecic from the start with follicular pustules and no scutula.

Favus of the scalp evolves steadily towards a cicatricial alopecia and in an old case one sees large bare scarred areas with a few odd tufts of hair and some crusting or scutula at the margins.

The skin may be affected and rarely lesions are generalized; typical scutula are produced. The nail changes are not clinically distinguishable from those produced by other fungous infections.

and is red and inflamed and may show thrush like lesions. There is a yellowish discharge containing white flakes in which cells and filaments are to be found. The skin of the vulva, thighs and perineum may be involved and show maceration



Fig. 223
Monilial vulvo-vaginitis.
Department of Gynaecology, University of Pretoria

erosion and pustulation. Itch is constant and usually severe (Fig. 223).

In rare cases the husband of a sufferer may develop balano-posthitis which heals spontaneously but recurs after intercourse. Monilial balano-posthitis or circum-meatal erosion may occur in male diabetics.

THE SKIN. Cutaneous moniliasis commonly occurs in diabetics, in the obese and in those whose skin is macerated by frequent immersion in water.

Intertrigo is sometimes caused by candida infection. One variety, known as *erosio interdigitalis*, occurs between the fingers

this possibility is not so important as to constitute a contra-indication to such treatment

MUCOUS MEMBRANES Moniliasis of the buccal mucosa is known as *thrush* and is found in sickly infants and in elderly often cachectic, people. The lesions are small or large occasionally confluent, patches of a grey to creamy lightly adherent deposit on the mucosa when removed a red, shiny surface is disclosed. Any part of the tongue and buccal surface may be affected sometimes all of it including the angles of the mouth spread to the oesophagus, trachea and upper bronchi rarely occurs (Fig 222) Budding cells and filaments are seen in material scraped from the lesions.



FIG. 222
Moniliasis. Cheilitis and perlèche
[R. Vanbreuseghem]

A smooth atrophic looking tongue is a rare manifestation of moniliasis in elderly people This phenomenon is not universally accepted as a sign of moniliasis, but I have recently seen two such cases showing odd patches of thrush and perlèche as well respond with remarkable speed to treatment with nystatin

Perlèche which is usually due basically to dental malocclusion may be complicated by candida infection. *Hairy tongue* is reputed sometimes to be due to moniliasis, but the organisms are probably saprophytic

The amount of candida in the mouth is vastly increased in patients taking broad-spectrum antibiotics and such patients may develop symptoms of glossitis or stomatitis it is not certain whether these symptoms are referable to infection or to allergic reaction to the antibiotics.

Vulvovaginitis occurs commonly in pregnancy and with diabetes, but may supervene on mucosa damaged by over treatment of some other disease The vagina is first affected

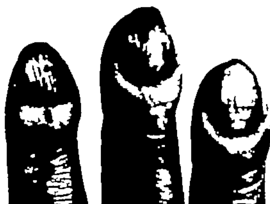


Fig. 225
Moniliasis. Paronychia and onychia.



Fig. 226
Moniliasis. Axillary intertrigo, part of generalized eruption in an obese woman.

as localized patches of violaceous erythema with maceration of the epithelium and sometimes vesiculation onychia and paronychia may be associated and the sufferers are usually women who work a great deal in water (Fig 224)

Monilial intertrigo is a rare variety of athlete's foot. The lesions are erythematous and moistly scaling Extension usually involves the dorsum of the toes and foot and flaccid vesico-pustules are seen at the margins



Fig 224

Moniliasis. Erosio interdigitalis.

[St John Hospital

Moist red smooth lesions with flaccid pustules or their scaly remains may be found in the groins axillae and submammary regions, diabetics and the obese are usually affected In some cases the moniliasis may be superimposed on some existing dermatosis and a therapeutic test is necessary to determine whether it is significant or not.

Perianal moniliasis is a rare cause of *pruritus ani* and is suspected when lesions like those described above are found Therapeutic test is necessary to establish the diagnosis

Onychia with paronychia is the commonest type of moniliasis in adults and occurs in those working much in water The nails are hard yellowish brown, thickened and furrowed but there is no subungual hyperkeratosis such as is seen with ringworm infections of the nails The surrounding skin is puffy red and painful or tender but very rarely suppurates. The nail changes are secondary to inflammatory changes in the matrix and are not caused by invasion by candida It is the rule for more than one nail to be affected and often all are involved (Fig 225)

finding of moniliasis will sometimes arouse the suspicion that diabetes may be present.

The prognosis in all types of superficial moniliasis has been greatly improved since the advent of the antibiotic nystatin (Mycostatin) which is usually much more effective than any other topical remedy. Even the stubborn paronychia responds in time to Mycostatin ointment provided maceration by water is avoided. Mycostatin powder may be better tolerated than ointment in some cases of intertrigo. A suspension of Mycostatin is used for buccal infections and pessaries for vaginitis. Other remedies that may be tried if Mycostatin fails or in the rare cases where it is not well tolerated are Dequadin (ointment and lotion) and Pruvagol cream. Gentian violet, the common application of the past, is messy and not very effective.

Oral Mycostatin need not be used unless the digestive tract is affected because it is not absorbed in quantity sufficient to affect skin lesions. Digestive moniliasis in adults is treated with Mycostatin tablets (1 or 2 each containing 500,000 units, 3 or 4 times daily) and in infants with a suspension (1 or 2 c.c., 100,000 units per c.c., before each feed). No side effects are reported.

Intravenous infusions of nystatin (200,000 to 400,000 units daily given over 6 hours) have been used for severe systemic moniliasis, but major side effects like those seen with amphotericin B are to be expected. Amphotericin B has also been used with success in systemic moniliasis.

ACTINOMYCOSIS

Infection with *Actinomyces israeli* causes a chronic suppurative granulomatous disease of the face and neck, of the chest or of the abdomen. The source of infection is almost always endogenous as the organism is a normal inhabitant of the mouth. The organism may enter the jaw through injured mucous membrane, be inhaled and cause lung and thoracic lesions or be swallowed and invade the intestinal mucosa. The precipitating factors and the reason why agricultural workers seem to be infected oftener than others are not known. Isolated lesions of organs such as the skin, bones, kidneys, etc., have been noted and visceral lesions are often seen when dissemination occurs from a primary infection of the face, chest or abdomen.

Generalized moniliasis of adults usually implies an extension of an intertriginous infection in which all the skin folds and the umbilicus participate The lesions have a distinctive pinkish-red colour and may be dry and glazed or moist peripheral scaling or flaccid pustules are found (Fig 226)

Infants may also develop generalized moniliasis which usually affects the great skin folds and often the scalp ears and face and limbs as well, occasionally the whole surface is affected. Chronic paronychia is frequently found and thrush is often present at the onset. The lesions are difficult to distinguish, except by trial of therapy from the diffuse bacterial infective eczemas of infancy The infection often passes to the infant from a vulvo-vaginitis in the mother In one case I have seen there was generalized erythema within two hours of birth and a typical eruption by the second day the mother had monilial vaginitis and had been admitted to hospital for delivery because her previous child was born with a skin disease which was rapidly fatal.

Treatment usually brings initial rapid improvement, but stubborn intertriginous lesions and paronychia often persist for months.

Rare cases are reported of a chronic dermatosis characterized by multiple filiform warty and horny growths containing large quantities of *C albicans* the significance of the fungus is uncertain and it may represent only secondary invasion of a naevoid hyperkeratosis

SYSTEMIC MONILIASIS

Bronchitis, pneumonia and gastro-intestinal disorders due to moniliasis are reported but the validity of the diagnosis is questioned

Disseminated visceral moniliasis with lesions in a variety of organs and with septicaemia meningitis endocarditis and bone and joint lesions is a rare manifestation of the disease

The diagnosis of moniliasis will often be retrospective since as already noted the demonstration of candida species by direct microscopy or by culture cannot be held to be convincing evidence of actual parasitic infection

Treatment The treatment of the primary condition which led to the development of moniliasis is of first importance The

Abdominal actinomycosis usually begins in the ileocaecal region and may give a picture suggestive of appendicitis. An abdominal mass forms and abscesses may point through the abdominal wall. The liver kidneys and vertebral bodies may be involved and the infection may spread up into the chest



Fig 228
Actinomycosis.
(L. J. A. Loewenthal—Lancet)

The disease is rarely diagnosed before laparotomy if the skin is not involved.

The diagnosis is made by finding the fungus in pus, sputum or scrapings from abscess walls or in biopsy specimens, and it is identified in anaerobic culture

Treatment. A mixed bacterial flora is found on culture in most cases of human actinomycosis and it is probable that the symbionts (e.g. *Staph. aureus* strains, *Actinobacillus actinomycetem comitans Bacteroides melaninogenicus* strains) are of aetiological importance. *A. israeli* is sensitive to penicillin and this should be given in doses of 2,000,000 units 8-hourly for six weeks, followed by 600,000 units daily for six weeks. The sensitivity of any symbiont should be determined and the appropriate antibiotic

Cervico-facial actinomycosis often begins in the lower jaw but the first sign of infection may appear at any point in the buccopharyngeal area including the tongue Eventually the soft tissues of the face and neck become swollen lumpy and hard The skin is bluish red as abscesses form and discharge



Fig 227

Actinomycosis.

([illegible])

through sinuses The pus contains little yellow granules which are masses of fungi Periostitis and osteomyelitis of the jaw and cranial bones may develop later (Figs. 227 and 228)

Thoracic actinomycosis begins with symptoms of subacute pulmonary infection and later abscesses develop in the lung often at the base The disease extends to the chest wall and subcutaneous abscesses and draining sinuses appear One or both lungs may be affected and the radiological appearances may suggest tuberculosis or a neoplasm The ribs are often attacked

deformity of the foot is produced as deep abscesses and fibrosis in the tissues and destructive and proliferative changes in the small bones appear. The patient, unexpectedly, suffers little pain, and generalized infection does not occur. Secondary infection is a great danger and is the cause of death in these cases.

Fungous elements can be seen and identified in the grains in the discharge and also in biopsy material and this serves to



Fig. 119

Left Actinomycotic mycetoma of knee due to *Nocardia brasiliensis*.
Middle Actinomycotic mycetoma of foot due to *Nocardia brasiliensis*.
(*R. Vanbreuseghem, G. Courtois, A. Thys and P. Dompierre*)
Right Maduromycetoma of neck.
(*R. Vanbreuseghem and M. Vandepitte*)

differentiate the disease from the other chronic granulomas and fungous diseases such as sporotrichosis and blastomycosis.

Treatment. Nocardial infections are treated with diaminodiphenyl sulphone, sulphonamides or antibiotics together with such surgical measures as may be indicated. When filamentous fungi are involved such treatment is ineffective except against secondary infection and excision or amputation are required.

NORTH AMERICAN BLASTOMYCOSIS (Gilchrist's disease)

This rare, chronic granulomatous disease occurs in the United States and occasionally in Canada. The causative organism, *Blastomyces dermatitidis*, has not been isolated in nature, but the source of infection in man is presumed to be exogenous: passage from man to man does not occur. Men are affected oftener than women and children.

given as well Surgical intervention is required only for large collections of pus in the pleural cavity or for the removal of scarred and bronchiectatic lung tissue remaining after treatment.

NOCARDIOSIS

Nocardiosis is a chronic granulomatous disease caused by various species of nocardia and producing lesions similar to those of maduromycosis and actinomycosis. The clinical types are (1) *mycetoma* a localized involvement often of the foot (which is one variety of Madura foot) and (2) *pulmonary and systemic* where the infection starts in the lungs simulating tuberculosis, and later becomes disseminated by the blood stream to the skin (abscesses and chronic fistulae) brain, and other organs. The organisms are seen in sputum pus and cerebro-spinal fluid as isolated elements or granules and are identified by aerobic culture

Treatment Diaminodiphenyl sulphone appears to be the most effective remedy now available Beginning with a daily dose of 300 mg (3 tablets) the dose is slowly reduced according to improvement and treatment must continue for many months. Sulphadiazine alone or with sulphamerazine (6 to 8 g daily) may be effective and streptomycin is useful in some cases. Surgical drainage excision of affected tissue or even amputation may be required

MADUROMYCOSIS (MADURA FOOT MYCETOMA)

A great variety of ascomycetes and fungi imperfecti have been shown to produce the condition commonly called Madura foot This is a disease of tropical and subtropical zones and the barefooted (almost always men) are usually affected the infection being introduced at a site of trauma. The foot is the commonest site of infection but lesions may be found elsewhere (Fig 229)

The early stages are rarely seen and when the patient presents himself it is usually with a swollen foot studded with granulomatous nodules and fistulae oozing viscid serum that contains characteristic granules of various colours This picture, which resembles that of actinomycosis, takes months or oftener years to develop and gross hard swelling and

Systemic blastomycosis begins insidiously as a chronic respiratory infection with symptoms suggestive of tuberculosis. When dissemination occurs there appear gummatous and ulcerative lesions in the skin and subcutaneous tissue and lesions may also be found in the bones, liver spleen, kidneys and elsewhere. The mortality rate is high.

The organism may be demonstrated in pus or in biopsy material as round, double contoured, budding yeast-like cells, and it can be cultured. Skin lesions show enormous epidermal hyperplasia, small abscesses in the dermis and epidermis and a granulomatous reaction in the dermis organisms are seen free in abscesses and in giant cells. Complement fixation tests and a blastomycin intradermal test are of less value in diagnosis than is demonstration of the organism.



Fig. 83

North American blastomycosis and the result of treatment for six weeks with amphotericin B Viable organisms were still present in the skin at this time

John D. [illegible]

Patients with blastomycosis may cross-react to histoplasmin and coccidioidin.

Treatment. Small localized lesions should be excised when possible Amphotericin B seems likely to prove the best remedy for this type of blastomycosis. Stilbamidine is sometimes effective and may still be useful in cases resistant to the antibiotic

Primary cutaneous blastomycosis is now known to be very rare and to occur usually after accidental infection in laboratory workers. A chancre develops at the site of inoculation and enlargement of the regional glands follows; the disease heals spontaneously.

It is likely that in most cases of blastomycosis the primary lesion is in the lung, but this lesion is often silent and only recognized if a radiological examination is made. Dissemina-



Fig. 230

North American blastomycosis.

[illegible]

tion of organisms from the lung may result in either localized lesions in the skin or in widespread lesions in a variety of organs, depending on the degree of immunity developed by the sufferer.

Secondary localized cutaneous blastomycosis. A solitary lesion is seen in most cases, with the face and extremities as sites of election. The original lesion is a papule or nodule that ulcerates and discharges pus. Slow peripheral extension produces ringed or serpiginous lesions with thick central scarring and elevated edges. The edges have a distinctive papilliform or verrucous appearance; they are purplish in colour and contain micro-abscesses (Figs. 230 and 231). This variety of the disease is rarely fatal.

ulcerate. The lungs are often involved by blood spread and lesions of other organs are described.

The yeast like budding organisms are found in pus and tissue specimens and identified by culture. Complement fixation and intradermal tests are of unproved value as aids to diagnosis.

Treatment. Sulphadiazine and sulphamerazine give good results in the superficial type but their effects are less spectacular in systemic infections. Autogenous vaccines are also recommended. Reports suggest that amphotericin B may be useful here.

Coccidioidomycosis

Coccidioidomycosis is an infectious disease caused by *Coccidioides immitis*, a soil saprophyte, which is inhaled in dust and commonly produces pulmonary lesions. The disease is endemic in the San Joaquin Valley of California (valley fever) and in other dry dusty areas in the United States and occurs sporadically elsewhere on the American continent.

In the endemic areas many inhabitants acquire the disease in an asymptomatic form as demonstrated by positive skin tests with coccidioidin in epidemiological surveys.

Primary pulmonary coccidioidomycosis when the infection is apparent, produces mild or severe symptoms of an acute respiratory infection or pleurisy. About 20 per cent of patients develop erythema nodosum on the shins and occasionally elsewhere 2 or 3 weeks after the respiratory symptoms subside. Urticarial and erythema multiforme-like rashes may also occur. Most sufferers recover but a few negroes in particular develop the progressive disease.

Progressive coccidioidomycosis develops within a few months of an attack of the primary pulmonary disease and proves fatal in about 50 per cent of cases after a few months to a year or so. The patient has fever and anorexia and rapidly loses weight. Dyspnoea and cyanosis result from consolidation of the lungs. Meningitis occurs in 25 per cent of cases. Abscesses, ulcers and verrucous and granulomatous lesions are found on the skin. Lesions may also be found in the bones, joints and other organs.

Primary cutaneous coccidioidomycosis is rare. In such cases a chancre develops at the site of inoculation, the regional glands

The total dose required is 4 to 6 g (or 6 to 10 g of the less toxic 2 hydroxy stilbamidine) given in daily intravenous infusions over about one month An initial dose of 50 mg is given in *100 c.c. of 5 per cent glucose over 1 hour on the* second day 100 mg and on the third and subsequent days 150 mg in 500 c.c over 3 to 4 hours The course may have to be repeated in some cases especially those of the systemic or disseminated type. Trigeminal neuralgia is a severe and frequent side-effect of stilbamidine treatment

SOUTH AMERICAN BLASTOMYCOSIS

This is a chronic granulomatous disease caused by *Blastomyces brasiliensis* and occurring in Brazil and other South American countries The source and manner of infection are unknown it is not contagious

Muco-cutaneous form The primary papular lesion is usually seen on the mucous surface of the mouth lips or nose or rarely on the adjacent skin The mucosal papule ulcerates and characteristic tiny red or yellow areas are seen on the surface Peripheral spread and invasion of deeper tissues takes place and new lesions appear in the surrounding mucosa until the epiglottis, vocal cords and uvula may be destroyed *Regional* lymph glands enlarge early become necrotic drain through the skin and form sinuses Lymph glands at a distance are affected by haematogenous spread of infection and behave similarly The lesions are very painful the patient has great difficulty in eating and dies in a few months to a year or two

Cutaneous form. This is characterized by gummatous, hyperkeratotic, verrucous and ulcerating necrotic *lesions the* face is most affected Keloid like lesions are seen in one type Lôbo s disease, found in the Amazon region of Brazil

Lymphatic form In this form the glands of the neck enlarge and become necrotic without visible primary infection of the mucosa

Visceral form The portal of entry is probably in the gastro-intestinal tract and the most extensive lesions are in the ileo-caecal region The liver and spleen enlarge and there is ascites. The superficial lymph glands enlarge but rarely

ulcerate. The lungs are often involved by blood spread and lesions of other organs are described

The yeast-like budding organisms are found in pus and tissue specimens and identified by culture Complement fixation and intradermal tests are of unproved value as aids to diagnosis.

Treatment. Sulphadiazine and sulphamerazine give good results in the superficial type but their effects are less spectacular in systemic infections. Autogenous vaccines are also recommended. Reports suggest that amphotericin B may be useful here

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Primary cutaneous coccidioidomycosis is rare In such cases a chancre develops at the site of inoculation, the regional glands

enlarge and nodules may appear along the lines of the lymphatics Spontaneous healing soon takes place and this helps to distinguish the primary cutaneous disease from the occasional case of the progressive type with an isolated skin lesion (where of course radiological examination of the lungs would disclose abnormalities)

The diagnosis is established by finding *C immitis* a non-budding thick walled spherule filled with enodspores, in sputum pus or biopsy specimens or by culturing the organism. Serum tests and an intradermal test with coccidioidin are useful in diagnosis and in estimating progress

Treatment. Until recently the treatment of progressive coccidioidomycosis was purely symptomatic, but amphotericin B appears to be effective in some cases

HISTOPLASMOSIS

The effects of infection by *Histoplasma capsulatum* are similar to those seen in coccidioidomycosis, ranging from a benign pulmonary form to a chronic, progressive and fatal disease Histoplasmosis is endemic in parts of the United States, and sporadic cases have been reported from most parts of the world.

Histoplasma capsulatum is a saprophyte in soil and commonly causes disease after its inhalation as spores in dust. Animals as well as man are affected but the disease is not contagious. Little epidemics have been reported in people demolishing buildings exploring caves or otherwise exposed to dust containing large quantities of spores

The organisms are ingested in the human body by phagocytic histiocytes and in the majority of cases the reticulo-endothelial system appears to be able to control and eventually *destroy the invaders without there being any* clinical evidence of disease It is interesting that many cases of overt histoplasmosis have occurred in patients suffering from diseases of the lympho-reticular system or tuberculosis

Benign pulmonary histoplasmosis is usually asymptomatic and heals spontaneously leaving multiple areas of calcification in the lungs and regional glands When symptoms are produced the picture may suggest tuberculosis or carcinoma

Localized superficial lesions usually ulcerative may rarely be found on the buccal mucosa penis or on the skin *It is*

uncertain whether such lesions are primary infections or result from spread from an inapparent lesion in the lungs. Their course is chronic, but eventual healing usually takes place and dissemination is not common.

Progressive histoplasmosis is rare and it is believed that the portal of entry of the causative organism is often in the mouth or gastro-intestinal tract and not the lung. Ulceration of the



FIG. 232

Progressive histoplasmosis. Patient died in adrenal failure and both adrenal glands were found to have been destroyed by histoplasmous growth

John D Knudsen

mouth and pharynx is often the first sign of disease in adults while children show fever, digestive disturbances, diarrhoea and emaciation as a result of ulceration in the gastro-intestinal tract. The liver and spleen enlarge and there is leukopenia and anaemia. Ulceration of the buccopharyngeal and genital regions is common and a great variety of cutaneous lesions may be seen including ulcers, abscesses, papules, purpura and vegetations (Fig. 232)

H. capsulatum is easily demonstrable in cases of the progressive type in blood, bone marrow, lymph glands or skin biopsy specimens. Serum and intradermal (histoplasmin) tests may assist in diagnosis and in epidemiological surveys.

Treatment Amphotericin B has given most encouraging results in histoplasmosis which has hitherto resisted all methods of treatment

CRYPTOCOCCOSIS (Torulosis)

This infection inappropriately known as European blastomycosis since distribution is world wide is caused by *Cryptococcus neoformans* which has a predilection for the brain and

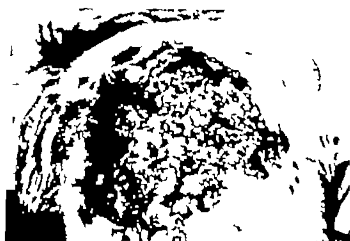


FIG. 233
Cryptococcosis of scalp.
[John D. [illegible]]

meninges The fungus usually enters through the respiratory tract, occasionally through the skin mucosa or intestinal tract and the disease begins with cough and fever or symptoms of meningitis Skin lesions are rare and usually result from dissemination from a visceral focus. Acneiform lesions, abscesses, pustules and ulcers occur and bone or gland lesions may point on the skin granulomatous lesions may occur on the buccal mucosa (Fig 233)

The organism is seen in infected tissues as an ovoid, single-budding yeast like organism surrounded by a wide gelatinous capsule It can be cultured and inoculated into mice

Treatment The prognosis is poor in untreated cases, but amphotericin B is often effective Cycloheximide (actidione) an antibiotic derived from certain streptomyces species is

highly active against *C. neoformans in vitro* but does not seem to be so useful as amphotericin B in practice

SPOROTRICHOSIS

Sporotrichosis is a chronic mycosis caused by *Sporotrichum schenckii*. Cases occur sporadically in most instances, but occasionally the disease becomes epidemic. The fungus seems to occur naturally on plants and trees and most sufferers are farmers, gardeners, etc., and develop the initial lesion on

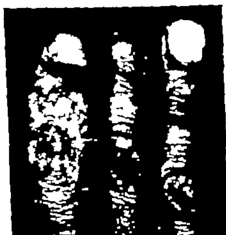


FIG. 231
Sporotrichosis. Healing primary lesion on finger of lumber worker
(John D. [illegible])

exposed skin. In a major epidemic among the mine workers of the Witwatersrand it was found that the fungus grew as a saprophyte on timber used as pit props. Human infection from affected animals is also reported. Sporotrichosis may remain localized in the skin or it may be disseminated by haematogenous spread.

The commonest clinical type is localized *lymphatic sporotrichosis* and this begins with a chancre at the site of inoculation on an extremity. This primary lesion is a bluish nodule which breaks down to form an indolent ulcer or a granulomatous or

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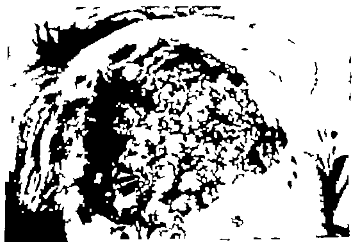


FIG 233
Cryptococcosis of scalp.
[John D Kirshbaum]

meninges The fungus usually enters through the respiratory tract, occasionally through the skin, mucosa or intestinal tract, and the disease begins with cough and fever or symptoms of meningitis Skin lesions are rare and usually result from dissemination from a visceral focus. Acneiform lesions, abscesses, pustules and ulcers occur and bone or gland lesions may point on the skin granulomatous lesions may occur on the buccal mucosa (Fig 233)

The organism is seen in infected tissues as an ovoid, single-budding yeast like organism surrounded by a wide gelatinous capsule it can be cultured and inoculated into mice

Treatment The prognosis is poor in untreated cases, but amphotericin B is often effective Cycloheximide (actidione) an antibiotic derived from certain streptomyces species is

scrofuloderma, secondary syphilis or folliculitis (Fig. 236). Superficial ringworm-like erythemato-squamous and bullous lesions are also described as occurring alone or with deeper involvement.



FIG. 236

Sporotrichosis. *Top* Nodules on leg. *Bottom* Part of disseminated frambœsiform eruption. Same patient as in Fig. 234.

John D. Kingsbury

The mucous membranes of the mouth, eyes and genitals may be affected primarily or secondarily and show erosive, ulcerative, vegetating or papillomatous lesions. Visceral lesions may arise in the liver, spleen, bones, muscles, kidneys and testicles.

verrucous plaque 2 to 5 cm in diameter. A few weeks later subcutaneous nodules appear above the chancre along the lines of the lymphatics and in time may climb up as far as the axillary or inguinal glands. The intervening lymphatics are sometimes palpable between the nodules. These nodules or gummas generally behave in the same way as the primary lesion and eventually ulcerate through the skin and lymph glands may also ulcerate (Figs. 234 and 235). There is a tendency towards spontaneous healing but untreated the lesions usually persist for months or years. The general health is unaffected.



Fig. 235
Sporotrichosis.
London Hospital

Haematogenous dissemination in cases of the localized lymphatic type is rare. In cases where this takes place there is often no recognizable primary lesion. One variety of disseminated sporotrichosis is *disseminated gummas*. There may be a few lesions or a hundred or more. In some cases no ulceration takes place and only subcutaneous nodules, doughy to the touch, are seen; incision releases pus and when the cut heals the abscess forms again. In other cases the gummas ulcerate and produce lesions of all sizes suggestive of tertiary syphilis, tuberculosis or ecthyma. Large abscesses of the hypodermal tissues, muscle and bone are sometimes seen.

Along with gummas may occur a great variety of cutaneous lesions that resemble those of sarcoidosis, lupus vulgaris,

scrofuloderma, secondary syphilis or folliculitis (Fig. 296). Superficial ringworm-like erythemato-squamous and bullous lesions are also described as occurring alone or with deeper involvement.



Fig. 296

Sporotrichosis. Top: Nodules on leg. Bottom: Part of disseminated framboesiform eruption. Same patient as in Fig. 294.

John D[illegible]

The mucous membranes of the mouth, eyes and genitals may be affected primarily or secondarily and show erosive ulcerative, vegetating or papillomatous lesions. Visceral lesions may arise in the liver, spleen, bones, muscles, kidneys and testicles.

Diagnosis is not difficult in the localized lymphatic type but in the disseminated variety all the granulomatous diseases and many others may be simulated The causative organism cannot be identified in pus or in biopsy specimens and diagnosis rests on cultures from pus from an unruptured nodule or from tissue Intraperitoneal injection of pus into mice and rats reproduces the disease and the organisms can be demonstrated in smears. The histological appearances are those of any chronic granuloma asteroid bodies are sometimes seen.

Treatment Potassium iodide is almost specific for sporotrichosis A solution containing 50 g in 250 c.c. should be prescribed a teaspoonful contains 1 g Dosage begins at 0 5 g four times daily and is rapidly increased until the patient is taking a total of 5 to 6 g a day The dose is taken in a large glass of water or milk. Treatment continues for a month after apparent cure to avoid relapse. Abscesses should not be incised but very large ones can be aspirated if necessary If local applications are necessary 0 2 per cent iodine and 2 per cent potassium iodide in water can be used Antibiotics may be required for secondary infection

For cases resistant to or patients completely intolerant of, potassium iodide intravenous arsenic, isoniazid sulphones and vaccines, stock or autogenous should be tried

CHROMOBLASTOMYCOSIS

Chromoblastomycosis (chromomycosis, dermatitis verrucosa) is caused by a variety of fungi of which *Hormodendron pedrosoi H compactum* and *Philophora verrucosa* are the commonest. The name of the disease is misleading since the clinical lesions have no characteristic colour (the fungi look brownish in unstained tissues) and the organisms are unrelated to the blastomyces Lesions are almost invariably solitary and found on the exposed skin of the limbs, face or neck. The fungi are probably introduced by trauma involving wood the majority of cases seen in South Africa occur in negro miners

The primary lesion is an itchy papule that enlarges peripherally to form an elevated dark red or bluish (black on negroid skin) verrucous patch (Fig 237) The disease is slowly progressive and new lesions appear around the original, some remaining discrete others running together to produce large

plaques. Pedunculated lesions are sometimes seen and secondary infection may cause ulceration, but usually the plaques remain dry and reminiscent of verrucous tuberculosis. Over many years a whole limb may be affected and elephantiasic swelling may follow on lymphatic obstruction.

Spontaneous healing is rare. The disease usually remains confined to the skin. Metastasis may occur to distant parts of the skin or very rarely to muscle but secondary involvement of viscera has not been reported and the general health is unaffected.

The term *mossy foot* is often aptly descriptive of the lesions of chromoblastomycosis, but this appearance may also be produced in lymphostatic verrucosis, filarial elephantiasis and yaws.

A diagnosis of chromoblastomycosis must be confirmed by demonstration of the causative organism. The fungi can be cultured and are visible in skin sections as groups of septate bodies in little abscesses in the dermis.



FIG. 137
Chromoblastomycosis.

Treatment. Small lesions may be excised or destroyed with the diathermy. Excision and plastic repair are required for large plaques if piecemeal attack by diathermy fails. Iodides are recommended for inoperable lesions, but I have not had any success. Local infiltration with amphotericin B solution is reported to cause regression of lesions. There is no need to amputate even a grossly affected limb which probably gives little trouble in a disease where metastasis is not to be feared.

RHINOSPORIDIOSIS

This disease is endemic in India and Ceylon, but sporadic cases have been reported from most parts of the world. The

cause is *Rhinosporidium seeberi* and the sites of election are the mucous membranes of the nose eyes ears and larynx, and occasionally the vagina and penis The skin may also be involved Young people are usually affected, males oftener than females

The nose is oftenest attacked, and polypoid papillomatous tumours develop on the mucosa and grow so that they protrude from the nares over the lip or backwards into the pharynx. These tumours are soft, mucoid and pink to dark red in colour and the whole surface is dotted with tiny white spots (sporangia) they bleed easily



Fig. 238
Rhinosporidiosis.
[F R Kirkland Allen]

The conjunctiva is frequently affected sometimes alone and the lesions are small pink flattened papules studded with sporangia As they enlarge they darken in colour Both bulbar and palpebral conjunctiva and the lachrymal sac may be affected

Soft papillomatous growths sometimes of considerable size appear on the skin (Fig 238) Polypoid lesions occur in the ear Warty papillomatous and polypoid growths are seen on the anogenital region. Metastastatic spread does not occur

Spontaneous cure is unlikely and the disease may last for very many years without seriously incapacitating the patient.

Sporangia and spores can be seen in the affected tissues, but the organism has not been cultured

Treatment The lesions must be widely excised preferably with diathermy to avoid spread of infection Antimony as Neostibosan 0 3 g daily to a total of 2 to 4 g may be used in addition to surgery

CHAPTER XVII

DISEASES DUE TO ANIMAL PARASITES

SCABIES

SCABIES, or the itch is caused by infestation of the skin by a mite, *Sarcoptes scabiei hominis* It is an extremely common disease in all parts of the world affecting especially those living unhygienically in close quarters In wartime for obvious reasons, the incidence of the disease always increases. Scabies is almost always transmitted by direct contact at night and in bed (it is often a venereal disease) but children may contract it when playing with infected companions. The chances of infection from clothing or bedding have been shown to be slight. Propagation takes place by the passage from one person to another of a gravid female or by larval nymphs or adult mites of both sexes.

The incubation period between contamination and first symptoms varies between 11 and 25 days in most cases infected for the first time in cases of reinfection symptoms often appear almost at once as a result of previous sensitization. The gravid female mite tunnels her way into and through the deeper layers of the stratum corneum, laying eggs at the rate of 1 to 5 a day during a life of 6 to 7 weeks. Such tunnels, known as burrows or runs, may be visible as fine sinuous white or greyish-black (from excrement) lines on the fronts of the wrists, the webs and sides of the fingers and, especially in infants, the palms and soles Eggs hatch in about three days producing larvae which emerge and travel over the skin to follicle openings where they burrow into the horny layer of the epidermis. Larvae moult to produce nymphs which moult again, once to produce adult males or twice to produce adult females. Males are rarely seen they die two days after copulation. The life cycle from egg to unfertilized female is 7 to 14 days.



Fig. 239
Scabies.



Fig. 24
Scabies. P pules on glans penis.

Fertilized females make for particular areas of skin where they burrow in to lay their eggs and never emerge again. These areas are the wrists, fingers, palms and soles, where the typical

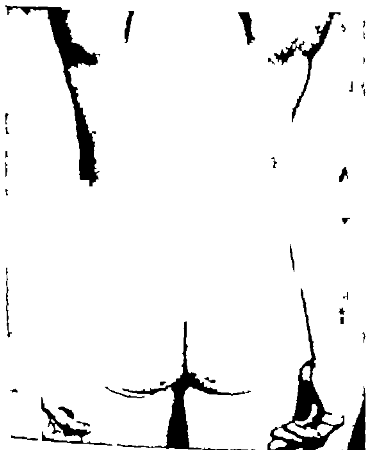


Fig. 24
Scabies. Papules on elbows and buttocks.

burrows are produced, and the extensor aspects of the elbows, the genitals, buttocks and anterior axillary folds, where papular lesions are seen. The greatest numbers of mites are found about the hands (Figs. 239, 240 and 241)

The lesions of scabies are widely disseminated and their quantity bears no relationship to the numbers of adult mites

which in the average case amount to no more than about a dozen Most of the lesions result, apparently from sensitization to the mites which becomes evident about a month after contamination The death rate of the mites at all stages is very high

The lesions of scabies are of two types, specific and ✓non-specific, the former relatively few and the latter generally numerous both may be modified by scratching eczematization and secondary infection

Specific lesions include the burrows already described and little pearly vesicles seen especially between the fingers and on the fronts of the wrists The vesicles are thought by some to result from prebuccal digestion of the skin by the mites.

Non-specific lesions are little acuminate papules which soon become scratched and scabbed

The distribution of the lesions is a major characteristic of the disease and of the greatest value in diagnosis. Sites of election are the interdigital spaces and the fronts of the wrists (burrows and vesicles) the backs of the elbows anterior axillary folds around the nipples in women the waist and umbilicus, penis and scrotum the buttocks near the natal cleft and the ankles and soles (burrows and vesicles in infants) The face and scalp are always spared except in infants and there are generally very few lesions on the back. Burrows are sometimes recognizable on the glans penis, but the common and very suggestive lesions on the male genitalia are large domed, scratched papules. Similar large papules, which are caused by gravid female mites may be seen at the elbows and axillae Scratched eruptions round the nipples in women (apart from pregnancy and lactation) should always suggest scabies

The lesions of scabies itch violently especially when the patient becomes warm in bed at night. Secondary pyoderma is the rule in the unclean and impetiginous and ecthymatous eruptions are common Eczematization may be due to microbic sensitization or to medicaments applied in treatment Transient albuminuria has often been observed in cases with severe secondary infection

Scabies shows little tendency to spontaneous cure and may persist indefinitely with attenuated symptoms. If one

member of a household is affected the others usually develop the disease in time.

The diagnosis is made on the basis of nocturnal itch the distribution of lesions and the finding of typical burrows or suggestive large papular lesions and is obvious if more than one member of a family is affected. When lesions of the genital region in men predominate syphilis may be suggested and it is important to remember that a superinfection with syphilis is far from rare in such cases which should be followed up for long enough to confirm or deny the possibility

With practice it becomes easy to demonstrate mites in burrows either by slitting them up with a needle and picking out the parasite or by shaving off the whole burrow and examining it (in 10 per cent potassium hydroxide under a cover slip) microscopically

Treatment. The treatment of scabies takes precedence over that of any complications which may be present even though a temporary aggravation of symptoms may result.

The best method of treatment is that with a 25 per cent benzyl benzoate emulsion (e.g Ascabiol) After a hot bath the lotion is applied all over the body from neck to toes this dries in a minute or two and then a second coat is applied This procedure is repeated the next night and on the following morning the patient puts on fresh underclothing and the old clothes and bed linen are boiled. If this treatment is done properly the chances of failure are negligible It is advisable to insist that all members of a family whether showing lesions or not, should be treated at the same time as the sufferer Itch usually diminishes markedly after the first night and disappears within a few days lesions heal in 7 to 10 days. Any residual itch should be treated with calamine lotion. Complications are treated symptomatically Eczematized lesions may be worsened by the treatment and the treatment itself may cause eczema. It is important not to mistake eczema after treatment for unhealed scabies and to aggravate it by further specific applications if in doubt, treat as eczema and watch.

Sulphur ointment, 10 per cent, applied after a bath every night for three nights is also effective, but messy and often irritating the patient wears the same suit of pyjamas under his clothes throughout the treatment period

NORWEGIAN SCABIES

This variety of scabies also caused by *Sarcoptes scabiei hominis* is characterized by a generalized scaly erythroderma with thick and even massive hyperkeratotic crusting especially about the hands, feet and elbows.

Crusty lesions may also be seen on the face and scalp. In these cases there are innumerable mites which can be seen very well in sections of the crusts which look like pumice stone full of locules containing the mites

Norwegian scabies does not apparently develop as a chronic form of ordinary scabies, but presents its typical lesions from the start the reason must be a difference in the host and not in the parasite The condition was first described in lepers and it usually occurs in people living in a state of material and physiological misery It has occurred with syringomyelia, mongolian idiocy and other mental or nervous diseases and is said to be relatively frequent in Brittany It is extremely contagious and very chronic.

Treatment is by removal of the crusts and the application of benzyl benzoate emulsion

ANIMAL SCABIES

Humans are occasionally infected by contact with animals suffering from scabies due to mites not identical with those normally affecting man. Cats and dogs are the common offenders but horses, sheep goats, pigs, fowls camels and even lions and llamas have been sources

The itchy papular rash appears less than a day after contact with the affected animal and is usually confined to the areas of contact, but may become disseminated If there is no further contact the lesions usually disappear in a few days without specific treatment, but benzyl benzoate is effective in stubborn cases

OTHER DISEASES DUE TO MITES

Grain itch and *grocer s itch* are due to a variety of mites found in grain cheese dried dates and figs, copra, tea, etc Farm workers dockers grocers and others who handle these substances sometimes develop itchy erythematous papular vesicular or urticarial eruptions on the exposed skin or shoulders

(from carrying sacks) New straw mattresses may also harbour mites. The number of cases is small in proportion to the distribution of the mites, and it is probable that contact sensitization or primary irritation in susceptible subjects is more important than actual bites. Lesions on the face often help to distinguish such eruptions from scabies The rash soon disappears when the worker is no longer in contact with the infested material. Such mites may also cause bronchitis and asthma as a result of inhalation of dust containing them

Similar rashes are also caused by *harvest bugs* larval forms of *Neotrombidium pusillum* which are common in late summer and autumn on grasses and shrubs in many parts of the world The lesions, which result from prebuccal digestion of the skin, are at first urticarial and later small papular The legs are often affected, but any part of the body may suffer as the mites climb along the limbs on to the body Scrub typhus is transmitted by one group of the species. Treatment is symptomatic, but protection is afforded by smearing sulphur ointment on the skin.

Fowl mites cause itchy papular eruptions on any part of the body People handling poultry and other birds are affected. Treatment with benzyl benzoate emulsion, as for scabies, is effective.

Blood-sucking *rat mites* may cause a scabies-like eruption The lesions are itchy scabbed papules of the scalp neck, back and axillae. Benzyl benzoate is curative.

Spider bites

Spider bites cause local pain and swelling and occasionally a gangrenous spot. Severe general symptoms may follow the bite of the female black widow or button spider (latrodectus species) Localized and generalized muscular spasm and cramps with chills, vomiting delirium and collapse appear shortly after the bite and an abdominal catastrophe may be simulated.

Treatment Application of a tourniquet (if possible) incision of the sting and *suction should be done at once.* Antivenom can be given if available ACTH and corticosteroids are used for severe reactions.

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Treatment. Application of a tourniquet (if possible) incision of the sting and suction should be done at once. Antivenom can be given if available. ACTH and corticosteroids are used for severe reactions.

Tick bites

Tick bites may cause urticarial papular and necrotic lesions Sometimes a chronic inflammatory papule showing a histological picture of eosinophilic dermal infiltrate and pseudo-epitheliomatous hypertrophy of the epidermis remains for months or years

Rickettsial diseases are transmitted by ticks and it is probable that *Ixodes ricinus* serves as the vector for an infective agent which causes erythema chronicum migrans and acrodermatitis chronica atrophicans.

An acute ascending polyneuritis tick paralysis, may result from the bite of a gravid female ixodid tick. One limb is generally first affected but the paralysis may spread until the tick is removed and may even prove fatal

LICE

Three varieties of lice, the related *Pediculus capitis* and *P corporis* and *Phthirius inguinalis* infest man Lice do not thrive long away from man as they live entirely on blood. They act as vectors of rickettsial diseases

Head lice

These are greyish brown insects 2 to 4 mm in length that infest the scalp especially at the nape of the neck and temporal regions and sometimes the eyebrows and eyelashes. Their nits or ova are little oval white or grey bodies firmly attached to the roots of hairs. Ova are much more numerous than lice Women and children are oftenest affected

Itch often leads to excoriation and secondary crusting and impetigo of the scalp with enlargement of the retro-auricular and cervical lymph glands The hair may become matted and ropy with pus and crusts forming a plica polonica

Treatment In profuse infestations it is wisest to begin by clipping the hair short Lethane 384 gives excellent results it is mixed with an equal quantity of liquid paraffin and about 8 c.c. of the mixture is massaged into the hair and scalp and left for 8 to 10 days without washing so that the lice emerging

from the ova will be killed (ova hatch in a week) DDT powder or emulsion (5 per cent) applied daily for a few days and then left for a week without washing is also effective

Body lice

These are similar in appearance to head lice but are rarely seen on the skin they and their ova are found in the seams of clothing Bites produce wheals and papules, soon disguised by scratch marks, especially at clothing pressure points. In long-standing cases the skin becomes pigmented lichenified and crusted, a condition known as vagabond's disease.

Treatment. Mass delousing is accomplished by blowing DDT powder under clothing with a spray gun Individual cases are treated by disinfestation of clothing by heat and the subsequent use of DDT powder

Pubic lice

Pubic lice are crab-like insects generally found about the pubic region and sometimes on the thighs, abdomen, axillae eyelashes or elsewhere. Lice and nits on the hairs are usually easily discovered. Itching is often severe but visible lesions are uncommon. Blue macules, maculae caeruleae up to 5 mm. in diameter are seen in some cases and may persist for several months. Infestation often occurs during sexual intercourse

Treatment is as for head lice

Bed bugs

The lesions resulting from the bites of the bed bug *Cimex lectularius*, are usually urticarial with a central red punctum haemorrhagic bullae may develop The lesions, which are discovered in the morning, as the bugs bite during sleep, are often grouped on the ankles or buttocks and are seldom numerous. Occasionally the appearance of papular urticaria, as seen with flea bites, is produced.

Infected houses are best treated by an experienced operator with DDT or hydrocyanic acid gas. The wary traveller can avoid attack in suspect dwellings by sleeping with the light burning

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Dimethyl phthalate (Mylol) or an ointment containing five drops of liquor cresoli saponatus in one ounce of Vaseline may be applied daily as repellants.

Myiasis

Cutaneous myiasis is the infestation of the skin by larvae of flies. The eggs may be laid directly on skin or on soil or clothing and the hatching larvae attach themselves to and burrow for varying distances into, the skin causing inflammatory changes. Normal skin or mucosa or wounds may be affected

Wound infestation may be due to the larvae of horse-flies, flesh-flies and bot or warble flies. The larvae feed on rotting tissues and in the case of *Cochliomyia hominivorax* may even invade bone.

Furunculoid lesions are caused by the larvae of *Dermatobia hominis* (eggs attached to the body of a biting mosquito) in South America and of *Cordylobia anthropophaga* (tumbu fly) in Africa. The lesions are generally thought to be boils until after about a week, maggots emerge from central puncta. They are usually few in number but I have seen one case in South Africa with lesions so numerous as to suggest a diagnosis of chickenpox. The maggots may be extracted entire or better left to emerge spontaneously and any secondary infection treated with local or systemic antibiotics.

CREEPING DISEASE

Creeping disease (larva migrans, myiasis linearis, sand-worm, etc.) is caused occasionally by the larvae of the horse bot-fly *Gastrophilus* and *Hypoderma*, the cattle-grub, and rarely by other larvae. The vast majority of cases are due to larvae of *Ankylostoma braziliense* or *Ankylostoma caninum*, the hookworms of cats and dogs.

The larvae enter the skin from moist soil or sand contaminated with dog or cat faeces and the sites of election are the feet, buttocks and genitals and, less often, the hands and other parts of the body. Children are affected oftener than adults and, in South Africa at least, white people much oftener than negroes.

FLEAS

Fleas are important as intermediaries in the spread of diseases such as plague (rat flea) and possibly tularemia and typhus Man is usually bitten by human (*pulex irritans*) cat and dog fleas The lesions are urticarial and usually grouped, but may be widespread especially in children causing papular urticaria.

DDT powder is used in control sprayed on carpets, furniture bedding basements and dogs and cats sleeping quarters

Tungiasis

The lesions of tungiasis (chigo itch chigger nigua, etc.) are caused by the burrowing of the gravid female sand flea, *Tunga penetrans* into the skin The disease is commonly seen in Central and South America and the West Indies, where it probably originated and in tropical Africa and parts of India. The insects live in dry soil and feed by sucking blood from man pigs, chickens and other animals Gravid females penetrate the skin and swell enormously as their ova ripen before being ejected

Lesions are commonest about the feet and under the toenails but may also be found on the buttocks, hands and elsewhere The primary lesion is a hard itchy subcutaneous nodule with a central black dot formed by the flea's two posterior abdominal segments Suppuration follows and a large pustule forms. Solitary or multiple lesions sometimes aggregated into plaques with a honeycomb appearance may be seen If the flea is not removed it is eventually extruded when the pustule ruptures and a deep ecthymatous ulcer is left. This may heal slowly or from it may develop cellulitis, gas gangrene septicaemia or tetanus The death rate from complications is high

Treatment The fleas must be removed entire and intact by enlarging the hole in the skin with a needle and then applying pressure Antibiotics locally or systemically are used if required Shoes or boots must always be worn in infested areas and the feet especially near the nails, inspected daily

LARVA CURRENS

This is the name suggested by Arthur and Shelley for a variety of creeping disease caused by the larvae of *Strongyloides stercoralis*, an unsegmented roundworm infesting the intestinal tract in man. Larvae may penetrate the skin enter the circulation and traverse the lungs on their way back to the gut. Skin



FIG. 243
Creeping disease Larva migrans.

of L. Murray Deft

lesions are usually perianal The larvae advance rapidly through the skin exciting a broad band of urticarial swelling as they go. Recurrent attacks may be noted

Treatment with dithiazanine is effective against strongyloidiasis.

OTHER DIRECT BITES AND MISCELLANEOUS IRRITATIONS

There is rarely any difficulty in recognizing the bites of mosquitoes, bees, wasps, midges, etc. The lesions may be urticarial, papular or occasionally haemorrhagic or bullous.

The lesions produced by the burrowing larvae are red tortuous linear tracks, 1 to 2 mm wide that may lengthen as much as an inch or more in the course of a day (Figs. 242 and 243) One several or dozens of tracks may be seen on a patient. Itching is severe and secondary coccal infection is the rule In relatively uninfected cases, apart from the tracks, there is often an erythematous papular eruption in the affected area probably the result of an allergic reaction Loeffler's syndrome of transient infiltration of the lungs with eosinophilia may occur The vast majority of cases tend to spontaneous cure in 4 to 6 months but some may persist much longer



FIG. 242
Creeping disease Larva migrans
(Vol L. Mason)

Treatment In young children and in cases where the tracks are very numerous or indistinct as a result of secondary infection Hetrazan (Banocide) should be tried the dose is 6 mg per kilo thrice daily for ten days At best this cures the condition and it always seems to have some sedative or larvistatic effect Antibiotics may be given at the same time for secondary infection and phenol and menthol ointment for itch

If the tracks are few and clearly visible the best treatment is to freeze an area of skin one inch in diameter with the end of the track as its centre with carbon dioxide ice the skin of the palms or soles must be frozen hard for two minutes the skin elsewhere for one minute Ethyl chloride spray may be used if dry ice is not available a cardboard template is used to protect the skin around the area to be frozen

Many other local and systemic remedies have been advocated, but none has proved satisfactory in my hands

Sea bather's eruption is a papular erythematous rash due presumably to irritation by some microscopic marine organism and encountered on the Florida coast and in the Bahamas.

Treatment for all the above conditions is symptomatic with soothing lotions, antibiotics for secondary infections and ACTH or cortisone for severe systemic reactions.

ONCHOCERCIASIS

This disease is endemic in tropical Africa and in Guatemala and southern Mexico. The skin and eye lesions are caused by

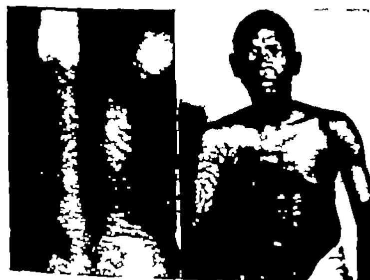


Fig. 243
Onchocerciasis (Uganda)

(W. H.

adult and microfilarial forms of a nematode, *Onchocerca volvulus*, which is spread by small biting gnats of the species simulium. In endemic areas white men are much less often affected than are negroes.

Two to ten months after the bite of an infected fly there appears, almost invariably, a nodule (onchocercoma) containing one or more adult worms. Fecundation of female

Severe reactions with shock or as a result of pharyngeal or laryngeal oedema may occur with bee and wasp stings, presumably as a result of sensitization

In the Middle East an urticarial and bullous eruption of the exposed parts due to bites of *Phlebotomus papatasi* is known as *harara* Infants and immigrants are affected and at first old bites flare up each time there are new ones most people eventually become immune



Fig. 244
Linear eruption caused by contact with jellyfish tentacle.

The sheep ked, *Melophagus ovinus* is a wingless blood sucking fly that causes haemorrhagic papules in wool sorters, shepherds etc.

The bites of scorpions and some centipedes may cause painful brawny oedematous swellings and lymphangitis.

Contact with caterpillars may be followed by itchy urticarial or polymorphous erythematous eruptions produced by their hairs and not by bites Cocoons also contain shed hairs and may produce rashes.

Larval beetles may cause contact dermatitis, and bullous eruptions result from crushing on the skin some beetles that contain cantharides

Contact with some jellyfish causes, at first, urticaria and when this subsides, eczematous lesions that may take a few weeks to subside (Fig 244) The lesions are almost always linear Shock is not uncommon with multiple lesions.

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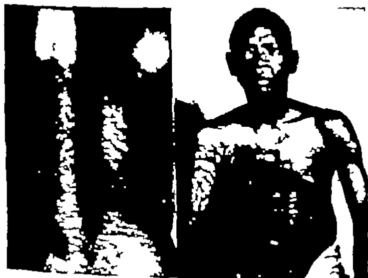


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(P. W. Ruben

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and often make for the conjunctiva (where they may be seen) and the region of the eye generally The most important skin lesions produced are the "Calabar swellings" which are oedematous urticarial swellings that persist for a few days and then disappear (Fig 246) Cystic swellings containing adult worms have been found in the viscera at autopsy

The disease may persist for at least fifteen years and signs may first appear long after a person has left tropical Africa. The diagnosis is made by finding microfilariae in the blood (collect between 10 a.m. and 2 p.m.) or by seeing an adult worm in the conjunctiva.



Fig 246
Loiasis.

Treatment. Good results are reported with Hetrazan (Banocide) 6 mg. per kilo thrice daily Three or four courses of 10 to 20 days are required. Removal of adult worms under local anaesthesia is unlikely to effect a cure as the infection is usually multiple.

DRACONTIASIS

Dracontiasis Guinea or Medina worm, is an infection by a nematode, *Dracunculus medinensis* The disease is encountered from the Middle East to India, in the West Indies and Brazil and in parts of tropical Africa and America.

Man becomes infected by drinking water containing certain species of the water flea, cyclops, in which are larvae of the nematode. These larvae penetrate the stomach wall and reach maturity in the retroperitoneal connective tissue. After copulation the male dies and is absorbed the female makes her way to the dermis in a part of the body usually the foot or leg, which is likely to come in contact with water

worms takes place in the nodule and microfilariae spread later and can eventually be found in almost any area of the dermis

Violent itch and lichenification of the skin is commonly found in African cases (Fig 245) In the American type erysipelas-like rashes on the face and fever often accompany ocular lesions localized lichenification of the face and extremities may also occur In most cases there are one or several onchocercomas, fibrous nodules or tumours 1 to 10 cm. in diameter on the thorax or iliac crests in African cases, on the scalp neck or shoulders in American cases

Eye lesions include conjunctivitis, iridocyclitis, keratitis, etc and blindness may result. Microfilariae may be seen with the slit lamp in the anterior chamber of the eye Elephantiasis of the genitals may occur

The disease is rarely fatal but eye complications are a major hazard Adult worms can be demonstrated in the onchocercomas and microfilaria in the skin in their vicinity Live microfilariae can be seen under the microscope by tearing a piece of skin in saline to liberate them

Treatment Removal of nodules may help in some cases, but unfortunately not all adult worms are in nodules. Hetrazan (Banocide) in doses of 6 mg per kilo body weight thrice daily for twenty days often gives good results pruritus increases during treatment, but is helped to some extent by antihistaminics Suramin in divided doses to a total of 160 mg per kilo may also be effective toxic effects are fairly frequent.

Loaiasis

Loaiasis loa loa or Calabar swelling is a filarial disease of tropical Africa affecting both the white and black races. The adult worms *Filaria loa* are between 30 and 55 mm. in length and live in the connective tissues of man microfilariae can be found in the circulating blood in the daytime (especially around 1 p m) but do not appear to account for any major symptoms. The insect vectors of microfilarial *F loa* are flies of the genus chrysops (mango flies)

Adult worms wander about the connective tissues including that of the skin. They appear to be attracted by light and heat

throughout the tropical belt, especially in the Guianas, India, South China and the Pacific islands. Adult filariae live in the lymphatic glands and vessels of man and produce microfilariae which periodically appear in the peripheral blood, usually at night, to be taken up by night-biting mosquitoes of the species culex and anopheles. After evolution in the insect they are again able to reach man when he is bitten by the mosquitoes. A non-periodic form in the Pacific is spread by *Aedes scutellaris pseudoscutellaris* and *A. sc. polynesiensis*. In most cases infestation with these filariae causes no symptoms in spite of the fact that microfilariae may be found in the blood in large numbers.

Major symptoms are caused by lymphatic obstruction by the filariae, giving lymphatic dilatation and oedema, and by secondary coccal infections. The course of the disease can be divided into a stage of invasion with allergic manifestations, a stage of deposition of the filariae and liberation of microfilariae and a terminal stage of fibrosis and obstructive phenomena with the appearance of elephantiasis.

The onset is with painful swellings of the scrotum and limbs; fever, malaise and sometimes urticaria or erythema nodosum-like swellings may be seen. Lymphadenitis and lymphangitis are common, may be accompanied by erysipelas-like inflammation and may lead to early elephantiasis. Abdominal lymphatics may be affected and give peritonitis. Another manner of onset is with recurrent "filarial fever" easily mistaken for malaria.

In the second stage appear abscesses as a result of secondary infection of dead filarial deposits, enlargement of inguinal and femoral glands with varicosity of the surrounding lymphatics (varicose groin-glands), swelling of the scrotum (lymph scrotum) and leakage of lymph from enlarged channels on its surface, arthritis, synovitis, hydrocele, hyluria, chylous diarrhoea and chylous ascites.

The last stage of permanent lymphatic obstruction produces elephantiasis, commonly of the lower limbs and scrotum, sometimes also of the arms, mammae, vulva or circumscribed parts of the limbs. Elephantiasis follows repeated attacks of lymphangitis and coccal infection. The affected part may be enormously swollen and the skin becomes thick and verrucous.

The female is 80 to 120 cm in length and dies after discharging all her larvae through the skin

The first sign of disease, which appears a year or more after infection, is a blister on or near the foot, occasionally elsewhere, and sometimes fever and urticaria The blister ruptures and an ulcer forms in the centre is the tip of the worm and a fine protruding tube the uterus Application of water causes the ejection of a fluid containing larvae Extrusion of larvae takes several weeks during which time the worm can be felt and seen as a cord under the skin After parturition the worm dies and may be absorbed or become calcified Abortive attempts to remove the worm often result in cellulitis and sometimes severe anaphylactoid reactions Fatalities from complications are not uncommon. One or more worms may be present



Fig. 247
Dracontiasis.
[Sudan ...]

Treatment The method employed by natives is to douche the skin with water to make the worm emerge enough to be wound round a little stick and then over several days by continued douching and gentle traction and massage the worm is slowly extracted (Fig 247) If the worm breaks complications almost inevitably follow The worm may also first be killed by injection of 1 1 000 solution of mercury bichloride into its subcutaneous portion but this does not make it any easier to extract. Surgical dissection has also been recommended

FILARIASIS

Filariasis or elephantiasis is commonly caused by *W uchereria bancrofti* (*W malayi* in Malaya and Indonesia) and cases occur

CUTANEOUS SCHISTOSOMIASIS

Swimmer's itch is due to the penetration of the human skin by certain schistosome cercariae whose natural hosts are birds or mammals with snails as intermediate hosts. The disease is widespread throughout the world and affects swimmers or waders in contaminated, still, fresh water. It is not communicable and heals spontaneously after about a week.



FIG. 249
Bilharziasis.
[Department of Gynaecology, University of Pretoria]

A pricking sensation is felt as the cercariae penetrate the skin and after about an hour little red macules, later papules, appear. Itching is severe, but can be allayed with calamine lotion with 2 per cent phenol. Pigmented spots may remain for a time after healing. In some cases diffuse erythema, urticarial lesions, vesicles or even pustules may be seen. Vigorous towelling of the skin after bathing reduces the risk of infection.

The tissues below the knee are oftenest affected giving the condition known as plus-four leg or *pantalon de Zouave* and scrotal swellings may be enormous (Fig 248)

The diagnosis is usually obvious in the late stages. Microfilariae can often be seen in blood specimens taken at intervals



Fig. 248
Filariasis.

[D. C. McArthur]

from 9 p m to midnight calcified adults may be seen on x-ray plates or found in material from abscesses, etc. Elephantiasic swellings may be due to other causes such as chronic recurrent coccal infections and neurofibromatosis.

Treatment Hetrazan (Banocide) is specific for the microfilariae. It is given for 3 to 4 weeks at the rate of 6 mg per kilo thrice daily The gross manifestations require surgical treatment

Cutaneous schistosomiasis

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Fig. 297

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Bilharziasis occurs particularly in Africa and Asia. Man is a natural host for *Schistosoma mansoni* *S japonicum* and *S haematobium*, with water snails as intermediate hosts. Penetration of the skin generally passes unnoticed but premonitory signs may appear about six weeks after infection with fever urticaria joint pains, bronchitis diarrhoea enlargement of the liver and spleen and occasionally jaundice. This stage clears up in a few weeks to be followed eventually by typical bilharziasis of the bladder or bowel In the late stage ova are sometimes deposited in ectopic sites in the skin especially about the vulva, where warty granulomatous plaques and nodules arise the ova can be seen in sections (Fig 249)

The trivalent salts of antimony are used in treatment skin growths must be excised

Cysticercosis cutis

The intermediate host of *Taenia solium* is normally the pig but occasionally man may so serve By eating contaminated meat or by regurgitation of ova from a worm in the intestine ripe proglottides reach the stomach and develop into onchospheres that enter the circulation and produce cysts in various parts of the body The lesions produced *in the skin* are little firm, pea-size subcutaneous nodules. They are usually numerous, persist indefinitely and eventually become calcified. The scolex of the parasite is recognized in biopsy specimens

Hydatid disease

Man may become the intermediate host for the larvae of *Echinococcus granulosus* (*Taenia echinococcus*) as a result of eating food contaminated by dogs faeces Hydatid cysts form in the liver or lungs. Intact cysts may be a cause of recurrent urticaria Rupture of a cyst precipitates acute anaphylactoid symptoms.

Trichinosis

Trichinosis is caused by infestation with *Trichinella spiralis* and is generally contracted by eating smoked or uncooked pork. Adult worms live in the intestines and larvae penetrate to the muscles Infestation may be asymptomatic or rarely produce

a fulminating and often fatal illness. This is characterized by high fever and intense diarrhoea followed after a week by muscular pains and difficulty in deglutition and mastication. There is usually oedema of the eyelids and face, sometimes of the limbs and abdomen. Itch and miliary rashes are described. Death may occur in the first day or two or after several weeks. Dermatomyositis may be simulated.

Hookworm Infestation

Hookworm infestation or ankylostomiasis is caused by the human hookworms *Ankylostoma duodenale* and *Necator americanus*. It is commonest in tropical countries. Adult worms live in the intestine and ova are discharged with the faeces, develop in soil into larvae which can penetrate the skin of a new host and be carried through the circulation to the lungs. Penetrating the capillary walls they reach the bronchi, pass up the trachea to the pharynx and are swallowed and reach the intestine.

The first signs of infestation are seen about the feet (ground itch) after walking in contaminated soil. These are erythematous macules and papules that become vesicular and pustular. Anaemia, debility and a variety of other symptoms appear after a few months. Indolent, dirty necrotic ulcers are seen on the legs in some fully-developed cases.

Treatment. Tetrachloroethylene is now used, 3 to 4 c.c. for adults, 0·2 c.c. per year of age for children. No fats, oils or alcohol may be taken at the same time. A saline purge is given 2 to 4 hours later.

Cutaneous Amoebiasis

Infection of the skin with the protozoan parasite *Entamoeba histolytica* is invariably secondary to amoebiasis of other tissues and results from direct spread and not embolism. *E. histolytica* is a parasite of the human large intestine and may spread directly or by embolism to other organs; the liver is often invaded through the portal circulation. The skin is usually affected as a result of prolonged contact with infected faeces or faecal discharges from wounds or abscesses.

Skin lesions are seen in the perianal skin and around operation wounds or sinuses and often consist of deep, spreading,

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Skin lesions are seen in the perianal skin and around operation wounds or sinuses and often consist of deep spreading,

necrotic ulcers which show no tendency to spontaneous cure Firm subcutaneous swellings (amoebomas) that do not ulcerate may also develop especially in the perianal skin, and may be mistaken for neoplasms Pus formation does not occur without secondary coccal infection and the prognosis is worsened when this is present.

Amoebiasis should be suspected in any case of chronic ulceration or granuloma formation about the anus or around wounds communicating with the abdomen. Amoebae can be recognized in necrotic tissue taken from ulcers moistened with saline and examined microscopically

Emetine, chloroquine acetarsol terramycin and aureomycin are used in treatment.

LEISHMANIASIS

Kala azar (visceral leishmaniasis) oriental sore and American muco-cutaneous leishmaniasis are all caused by morphologically and culturally identical protozoa of the genus leishmania Natural hosts for the parasites are man dogs and many other small animals and the disease is spread generally by biting phlebotomus flies

Oriental sore

Oriental sore is endemic around the Mediterranean, in the Middle East North Africa, India and Asia The incubation period is generally long even several years Lesions are often solitary and on exposed skin, but up to 300 have been seen on a patient. The clinical pictures produced are of infinite variety

A common form is a small bluish red infiltrated papule that may heal in a few months or enlarge to a *boil like* ulcerated lesion that heals with scarring after 6 to 7 months. Non-ulcerating nodular lesions also occur

The furunculoid lesions often spread outwards as granulomatous infiltrates that may resemble the lesions seen in tertiary syphilis, lupus vulgaris, *lupus erythematosus or blastomycosis* the face is commonly affected in this variety (Fig 250)

Relapsing leishmaniasis appears as small yellowish to bluish sometimes scaling papules at the sites of apparently

healed lesions of the ordinary type. The papules may coalesce to plaques or form rings. The resemblance to lupus vulgaris is very striking and apple-jelly nodules may be seen on diascopy This variety may remain active for very many years.

Framboesiform, verrucous, eczematous and large ulcerative types are also encountered.

The term dermal leishmanoid is used to describe lesions appearing a year or two after apparent cure of kala-azar The



FIG. 230
Leishmaniasis. Oriental sore.

cheeks and forehead are oftenest affected, but the whole face or rarely other regions may be affected. Macular papular nodular and verrucous lesions may be seen. Kala azar and oriental sore rarely occur together

An attack of oriental sore usually confers immunity and attack of American leishmaniasis does not.

Parasites may be demonstrated in stained specimens obtained by scraping or pipette aspiration at the edge of a lesion. Cultures are made if such tests are negative, as they

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FIG. 25

American leishmaniasis.

(Orlando [illegible])

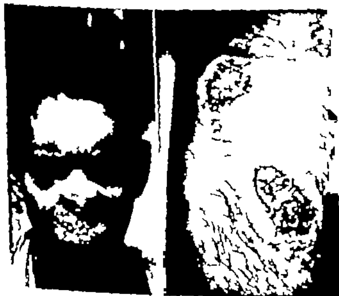


FIG. 25[illegible]

American leishmaniasis.

(Orlando [illegible])

may be in old or relapsing lesions An intradermal test using killed organisms may also be positive especially in the lupoid, relapsing cases the test remains positive for years after cure

American leishmaniasis

This disease is seen in South and Central America where it is known in different areas as forest or bosch yaws, pian bois, chiclero ulcer uta, espundia etc. It differs from oriental sore in affecting mucous membranes being more chronic and destructive resisting treatment and producing no immunity

The lesions have been classified by Rabello as follows

Cutaneous	A. Ulcerative	
		1 Impetiginoid
		2 *Ecthymatoid*
		3 True ulcerative.
	B Non-ulcerative.	
		1 Nodular dermal
		2 Vegetating frambœsiform or verrucous
Subcutaneous	A Non ulcerative nodular hypodermal	
	B Nodulo-ulcerative	
Mucosal	A Non ulcerative vegetating	
	B Ulcerative ulcero-vegetating	
Mixed	Combinations of those above	

Skin lesions begin at sites of insect bites as papules that develop into nodular ulcerative or verrucous lesions Generalization may result from auto-inoculation multiple infections or lymph spread. In a lymphangitic type nodules that eventually ulcerate appear along the lines of lymphatics on an extremity giving a picture like that of sporotrichosis (Figs. 251 252 and 253)

Mucosal lesions arise either from local spread of lesions on the face to the mouth or nose (uta) or *de novo* months or years after skin lesions have appeared (espundia) The latter form affects the buccal mucosa nose pharynx, larynx trachea, bronchi and oesophagus first with oedema later with soft granulomatous infiltrations Espundia progresses slowly towards mutilation and sometimes cachexia and death

Chiclero ulcers of the ears are seen in chicle collectors in Mexico and Guatemala the mucous membranes are not affected in this form.

Leprosy yaws, syphilis and the deep mycoses may all be simulated by American leishmaniasis diagnosis depends on demonstration of organisms by direct or cultural methods.

Kala-azar

Kala-azar is characterized by chronic irregular fever hypertrophy of the liver and spleen and in advanced cases, ulcerations of the digestive tract. Cancrum oris occurs with kala-azar in the Far East and the Sudan. Patchy melanin pigmentation of the face may be seen. Dermal leishmanoid (or leishmanide) occurs in treated cases.

Treatment. Vaccination with living cultures (into the thigh) is used in areas where oriental sore is hyperendemic. A great many remedies have been prescribed for leishmaniasis, but antimony salts seem to be the most reliable Degos speaks highly of glucantine (2 168 R.P) Antibiotics are ineffective. Among local treatments that may be tried are cauterization, injection of 0·05 to 0 1 g Mepacrine in 1 to 2 c.c. water into the lesions and radiotherapy Control of the insect vectors offers more hope of success in eliminating the disease than does treatment of established cases.

Trypanosomiasis

South American trypanosomiasis

South American trypanosomiasis Chagas disease, is caused by *Trypanosoma cruzi* and occurs principally in Brazil, the Argentine and Uruguay In Brazil the natural reservoir is the armadillo, elsewhere the otter and opossum The disease is spread to man by reduviid bugs whose faeces contain the parasites which are rubbed into the skin or conjunctiva. The disease is generally benign, but may be fatal in young children who are oftenest affected There are two forms of the disease, acute and chronic (which follows on the acute) but skin lesions are seen only in acute cases.

The acute disease begins 10 to 15 days after contamination with high fever swelling of the face and sometimes other parts



Fig. 253

American leishmaniasis.

[Orlando Canizares]

Chiclero ulcers of the ears are seen in chicle collectors in Mexico and Guatemala the mucous membranes are not affected in this form

Leprosy yaws, syphilis and the deep mycoses may all be simulated by American leishmaniasis diagnosis depends on demonstration of organisms by direct or cultural methods.

KALA AZAR

Kala-azar is characterized by chronic irregular fever hypertrophy of the liver and spleen and, in advanced cases, ulcerations of the digestive tract. Cancrum oris occurs with kala-azar in the Far East and the Sudan Patchy melanin pigmentation of the face may be seen. Dermal leishmanoid (or leishmanide) occurs in treated cases.

Treatment. Vaccination with living cultures (into the thigh) is used in areas where oriental sore is hyperendemic. A great many remedies have been prescribed for leishmaniasis, but antimony salts seem to be the most reliable Degos speaks highly of glucantime (2 168 R.P) Antibiotics are ineffective Among local treatments that may be tried are cauterization, injection of 0·05 to 0 1 g Mepacrine in 1 to 2 c.c. water into the lesions and radiotherapy Control of the insect vectors offers more hope of success in eliminating the disease than does treatment of established cases.

TRYPANOSOMIASIS

SOUTH AMERICAN TRYPANOSOMIASIS

South American trypanosomiasis, Chagas' disease is caused by *Trypanosoma cruzi* and occurs principally in Brazil the Argentine and Uruguay In Brazil the natural reservoir is the armadillo, elsewhere the otter and opossum. The disease is spread to man by reduviid bugs whose faeces contain the parasites which are rubbed into the skin or conjunctiva. The disease is generally benign, but may be fatal in young children who are oftenest affected. There are two forms of the disease, acute and chronic (which follows on the acute) but skin lesions are seen only in acute cases

The acute disease begins 10 to 15 days after contamination with high fever swelling of the face and sometimes other parts

of the body and tender enlargement of lymph glands Facial oedema is often unilateral, affecting the eyelids particularly when the infestation takes place through the eye and is accompanied by conjunctivitis, dacryocystitis and regional adenopathy

A primary skin lesion chagoma is sometimes seen and consists of a painful red papule that may develop into an infiltrated plaque on the face or neck healing may leave a retracted scar Urticarial erythematous and multiform generalized eruptions may also occur Other manifestations include hepato-splenomegaly and occasionally acute meningo-encephalitis The acute disease lasts a few days to a month or two and confers at least a degree of immunity

The chronic or cardiac, form is characterized by arrhythmia bradycardia, extra systoles and even heart block the central nervous system skeletal muscles and liver are also affected

Parasites can be demonstrated in fresh or stained peripheral blood films in the acute stage and by animal inoculation and other methods in the late stage

Treatment Bayer 7602 (Surfen) or the identical British product M 3 024 are used in the acute phase but are not very effective in the later phases when parasites are endocellular they are very toxic Antibiotics do not appear to have any specific effect

African Trypanosomiasis

African trypanosomiasis sleeping sickness, is caused by *Trypanosoma gambiense* and *T rhodesiense* Many animals are natural hosts for the parasites which reach man through the bites of tsetse flies (glossina) The incubation period is about 10 to 15 days and there may be local inflammation at the site of the bite and sometimes regional adenopathy Skin eruptions, trypanides may be seen in the early febrile stages of the disease they include patchy erythema papular eruptions and annular and large polycyclic erythemas Polyadenitis is frequent and some patients have an intolerable itch

The trypanosomes may be demonstrated in the peripheral blood, cerebro-spinal fluid or bone marrow directly or by animal inoculation

Treatment Bayer 205 (Germanin Suramin) and other complex urea compounds, arsenicals and antimony compounds are used in treatment.

BARTONELLOSIS

Infection with *Bartonella bacilliformis* may cause either an acute, severe and often fatal disease Oroya fever or a more benign and chronic disease verruga peruana transition forms



FIG. 54

Bartonellosis. *Verruga peruana.*

[illegible]

link the two. These diseases have been endemic in certain areas of Peru from time immemorial and were encountered in Colombia after the war with Peru in 1932 The source of the parasite in nature is unknown, but it spreads to man as a result of sand fly (phlebotomus) bites.

Oroya fever begins after an incubation period averaging 10 to 20 days with malaise, remittent fever and chills. A profound pernicious anaemia appears rapidly and is accompanied by leukaemia-like increase of leukocytes among which immature forms may be seen. Bartonella is found in

erythrocytes as rod-shaped or round bodies, singly in pairs or in chains (Giemsa stain)

Verruga peruana begins with an invasive stage, lasting a few months, of fever malaise and simple anaemia. As these symptoms improve the eruptive stage begins and miliary and nodular subcutaneous lesions are seen, the lesions appearing in crops Miliary lesions affect the extensor surfaces of the limbs particularly and begin as hard red papules some of which enlarge to about 0 5 cm diameter and become softer Such lesions are sessile or rounded and some become pedunculated (Fig 254) The overlying skin becomes wrinkled and haemorrhagic crusts may form The mucous membranes may be affected

Nodular lesions are seen on the limbs and may become as big as hens eggs trauma may cause serious haemorrhage Spontaneous cure occurs after a few months to a year and healing may leave no trace on the skin An attack confers lasting immunity

No specific treatment is known blood transfusion may be necessary

RAT BITE FEVER

Two conditions with similar symptoms but caused by different organisms may follow the bites of rats or other animals.

Sodoku is caused by infection with *Spirillum minus* a natural parasite of rats and some other rodents and occasionally cats, dogs and ferrets. Between 5 and 30 days after the bite there is a sudden onset of fever and malaise and the area originally bitten becomes inflamed and oedematous vesiculation necrosis and ulceration usually follow A generalized maculo-papular dusky erythematous rash and urticaria may also appear The original febrile attack lasts 3 to 4 days and then subsides to be followed by relapse after 6 to 10 days and relapses of diminishing severity may continue to appear for weeks or months in untreated cases Spontaneous cure with immunity is the end result.

Spirilla can be demonstrated after the eighth day in the blood of inoculated mice (patient s blood taken in a febrile phase) Penicillin is rapidly curative

Haverhill fever is due to infection with *Streptobacillus moniliformis*, and the disease usually follows rat-bites, and occasionally the ingestion of contaminated food, especially milk.

The incubation period is only 2 to 5 days and no ulcer develops at the site of the bite although this may swell. The rash is maculo-papular, morbilliform or petechial; arthritis commonly occurs. Urticarial lesions may be seen during recurrences.

The streptobacillus can be cultured from the blood and specific agglutinins are present in the serum. Penicillin is usually effective; other antibiotics may be tried for resistant cases.

CHAPTER XVIII

METABOLIC DISEASES

THE LIPOIDOSES

THE lipoidoses are a group of diseases due to local or generalized disturbance of lipid metabolism and characterized by lesions, in the skin or elsewhere caused by impregnation of the tissues with lipids. They are classified according to the nature of the lipid its distribution either intra or extracellularly and whether its value in the blood serum is normal or elevated. Thannhauser's classification is roughly followed.

A. Hypercholesteraemic xanthomatoses.
  1 Essential familial xanthomatosis.
  2 Xanthomatosis with liver disease.
  3 Xanthomatosis with hypothyroidism.
B Hyperlipaemia (neutral fat) with eruptive xanthomatoses.
  1 Idiopathic
    a Juvenile type (Bürger-Grütz)
    b Adult type
  2 Symptomatic in diabetes etc
C. Normocholesteraemic xanthomatoses.
  1 Lipid reticulo-endotheliosis
    a Letterer Siwe disease
    b Hand Schüller Christian disease.
    c Eosinophilic granuloma of bone
  2 Xanthoma cells in tumours
D Extracellular lipoidoses
  1 Lipoid proteinosis
  2 Extracellular cholesterosis
  3 Necrobiosis lipoidica
E Disturbances of phospholipid metabolism
  1 Nieman Pick disease (lecithin)
  2 Gaucher's disease (kerasin)

HYPERCHOLESTERAEMIC XANTHOMATOSES

ESSENTIAL FAMILIAL XANTHOMATOSIS

Essential familial hypercholesteraemic xanthomatosis is the commonest of the lipoidoses. The disease is inherited as a dominant trait and is characterized by the biochemical picture of high figures for serum cholesterol and sometimes phospholipids, but normal serum neutral fat. More important



FIG. 255
Xanthelasma palpebrarum.

than any cutaneous manifestations is the tendency for sufferers early to develop atherosclerosis with its attendant complications from vascular obstruction in various organs. A great variety of clinical pictures is produced in this type of xanthomatosis and note must be made, too, of *formes frustes* with hypercholesteraemia and atherosclerosis without cutaneous signs.

XANTHELASMA PALPEBRARUM. Xanthoma of the eyelids is a common disease affecting both sexes, women more than men. It usually appears after middle age and is accompanied in about 50 per cent of cases by hypercholesteraemia. The lesions are slightly-elevated, yellow papules or little plaques dotted about the eyelids near the inner canthi (Fig 255). Distribution is usually symmetrical. Other xanthomas may be found elsewhere on the skin.

Xanthoma of the eyelids may also be encountered in diabetes and in biliary disease. It is no longer dismissed as always a banal and unimportant disorder and its discovery should imply a search for its cause so that major complications may in some instances be averted

Treatment Tiny lesions may be destroyed by sparking with the diathermy but excision gives the best cosmetic results for large or multiple lesions

XANTHOMA TUBEROSUM This variety of xanthoma is less frequent than xanthoma palpebrarum with which it is often associated Hypercholesteraemia, often with very high values, is usually discovered Atherosclerosis is a frequent complication and vascular obstructive phenomena such as angina and coronary thrombosis may occur in young subjects, even in children and adolescents

The lesions appear at any age from early childhood and are commonest in young people. They are smooth yellow papules nodules, tumours or plaques symmetrically distributed on the extensor surfaces of the elbows or knees, buttocks, shoulders wrists heels or the dorsa of the fingers (Fig 256) Lesions are usually grouped on the sites of election but they may coalesce to form large sometimes pedunculated tumours which may interfere with joint movements. The tense over lying skin often shows telangiectases and may ulcerate.

Tendon sheaths (xanthoma tendinosum) and synovial membranes may be involved usually in association with skin lesions, sometimes as a solitary phenomenon The sheaths of the tendo achillis and of the extensor tendons of the hands are sites of election

Histopathology The characteristic feature of all xanthomas is the presence in the dermis of xanthoma or foam cells. These are large phagocytic cells that show in routine sections a vacuolated reticulate or foamy cytoplasm as a result of dissolution of the lipids they contained Their lipid contents cholesterol and phospholipids are demonstrable by fat stains in frozen sections. Xanthoma cells are histiocytes. They usually have one nucleus but may sometimes be very large and multinucleated Multinucleated cells may have the appearance of foreign body giant cells with irregularly-scattered nuclei or they may take the form of Touton giant cells where the

nuclei are centrally clustered round a small island of non-foamy cytoplasm and surrounded by foamy cytoplasm. In early lesions inflammatory cells may be present, in old lesions fibroblasts are seen.

Treatment of inaesthetic or troublesome lesions is by excision. Pressure strapping with adhesive bandage is reputed



Fig. 276

Xanthoma tuberosum.

[*Annales de Dermatologie et de Syphiligraphie*]

sometimes to cause involution of lesions about joints. The use of lipotropic substances has not so far been successful Very low fat diets may bring some amelioration of skin lesions and are of importance in the prophylaxis of vascular deterioration.

XANTHOMATOSIS WITH LIVER DISEASE

Liver diseases are very rare causes of xanthomatosis biliary cirrhosis, angiocholitis, haemochromatosis, obstruction

of the bile duct and chronic pancreatitis have been implicated, the first named being the most frequent.

In biliary cirrhosis the eruption of xanthomas follows on chronic jaundice The lesions are often small and widely distributed but tuberous xanthomas may be found at pressure points xanthoma palpebrarum is commonly found Linear lesions may be seen in the creases of the palms and soles. The liver and spleen are enlarged. Serum cholesterol values are high and neutral fat values normal Other skin manifestations in cirrhosis include chronic pruritus and sometimes, a recurrent papulo-pustular dermatitis The pruritus may yield to methyl testosterone, 10 to 30 mg daily administered sublingually

XANTHOMATOSIS WITH HYPOTHYROIDISM

Xanthomatous eruptions are occasionally found in cases of myxoedema Hyperlipaemia and hypercholesteraemia are demonstrable

Treatment of the myxoedema is followed by disappearance of the xanthomas.

HYPERLIPAEMIA WITH XANTHOMATOSES

IDIOPATHIC FAMILIAL HYPERLIPAEMIA

Juvenile familial hyperlipaemia Bürger Grütz disease or hepatosplenomegalic xanthomatosis is a disease of older children The manner of inheritance is uncertain The lesions erupt as papules or nodules in wide distribution and the lips, buccal and laryngeal mucosae may be involved Vesiculo-ulcerative eruptions with no foam cells are also encountered There is massive but fluctuating enlargement of the liver and spleen and patients may suffer attacks of abdominal colic Serum neutral fats and all the other serum lipids are increased.

Treatment is by low fat diets

Adult familial hyperlipaemia This is believed to be a minor late-developing form of the juvenile disease. Xanthomatous eruptions lipaemia and attacks of abdominal pain are the main features. Vascular obstructions may occur but such

complications are nothing like as frequent as they are in cases of hypercholesteraemia.

Treatment is by low fat diets.

Symptomatic hyperlipaemia with xanthomatosis

The commonest cause of symptomatic hyperlipaemia is diabetes mellitus, but it also occurs in nephrosis, pancreatitis and von Gierke's disease. The eruptive xanthomatosis that may follow is the same in all these diseases.

Xanthomatosis occurs in severe diabetes mellitus and may occasionally be the first evidence of disease. The yellow papules or little nodules erupt in crops in wide distribution. There may be an erythematous halo around the lesions and vesiculation or even ulceration may occur. Pruritus is common and may be severe. All the serum lipids are increased in quantity

Treatment of the diabetes cures the xanthomatosis.

NORMOCHOLESTERAEMIC XANTHOMATOSES

Lipid reticulo-endotheliosis

The diseases in this group are considered with the eosinophilic granulomas.

Xanthoma cells in inflammatory diseases and tumours

Foam cells containing cholesterol and other lipids may be found in chronic inflammatory infiltrates in the skin (e.g. in tuberculous cutis) or in other organs (e.g. osteomyelitis, breast abscesses) No disturbance of serum lipids is demonstrable and the source of the intracellular lipids is uncertain. They may either have been ingested by phagocytic histiocytes or elaborated by some intracellular enzymatic process.

Foam cells may also be demonstrable in some mesodermal tumours such as sarcomas, angiomas and naevi.

Naevo-xantho-endothelioma (*MacDonagh*) juvenile or congenital xanthoma, is a rare condition apparent at birth or appearing in early life. It is characterized by firm yellowish to reddish papules or nodules grouped on the points of the elbows or knees, shoulders, face or elsewhere. The serum lipids

are normal The lesions usually disappear spontaneously before puberty

Lever believes this to be a young histiocytoma histiocytes predominate in the infiltrate with foam cells, Touton and foreign body giant cells and capillary proliferation. Other authorities would classify naevoxantho-endothelioma as a variant of xanthoma or as a *forme fruste* of the Hand-Schüller Christian syndrome.

EXTRACELLULAR LIPOIDOSES

Lipoid proteinosis (hyalinosis cutis et mucosae)

Lipoid proteinosis of the skin and mucous membranes (Urbach Wiethe) is a rare hereditary (recessive) and familial



Fig 257

Lipoid proteinosis.

[University of Cape Town] *[J. P. Scott]*

disease that manifests itself in the first few months of life with symptoms of hoarseness or spasmodic dyspnoea from laryngeal stenosis Hoarseness is a feature of the disease at all ages. Visible changes in the skin and mucous membranes, produced by lipid infiltration, appear later in childhood or adult life

The skin lesions are elastic, yellowish papules or nodules grouped in plaques or in linear formation on the face, neck, scalp, knees, elbows and dorsa of the fingers warty and hyperkeratotic lesions may also be observed and, rarely bullous or pustular elements. The skin is fragile and scarring follows trauma (Fig 257)

The tongue is usually affected It is firmer and less mobile than normal. The epiglottis and vocal cords are thickened and infiltrated and nodular lesions may be found on the lips and buccal mucosa Infiltration of the genital mucosa and adjacent skin may be found in both sexes. Small papules may be discovered in the margins of the eyelids.

The blood lipids may be normal there may be an increase in total lipids or a relative increase in phospholipids. Diabetes, alopecia and intracranial calcification may be associated

Histopathology Epidermal changes of hyperkeratosis or acanthosis are of minor importance in comparison with the dermal changes. In the upper regions of the thickened dermis are seen thick, undulating bands of poorly-staining hyaline material running perpendicular to the epidermis. The hyaline material makes a thick mantle to the blood vessels. Deeper in the dermis the collagen is normal, but the hyaline material is still found around some vessels and sweat glands. Special staining shows much lipid material in droplets among the hyaline and especially near blood vessels the exact nature of the lipid is still unknown.

Differential diagnosis from amyloidosis of the skin or colloid milium may at times be extremely difficult. Prognosis as regards expectation of life is good.

Treatment in a general sense is unavailing, but surgical interference may be necessary for infiltrates in the laryngeal region.

EXTRACELLULAR CHOLESTEROSIS

This is a very rare chronic condition characterized by extracellular cholesterol deposits and by recurrent eruptions of reddish-brown plaques and tumours of the skin and mucous membranes. The serum cholesterol is normal in quantity

The primary lesions are little papules or vesicles that coalesce to form plaques. Sites of election are the dorsal

surfaces of the hands and feet and the extensor aspect of the legs

Histopathology There is a dense histiocytic and lymphocytic infiltrate the blood vessels are dilated and their endothelium swollen No foam cells are present but special stains show fat droplets in extracellular distribution especially about the blood vessels Fibrosis is evident in healing lesions.

The cause of the disease is unknown It is not universally accepted as a disease entity and some authorities consider it to be only a variant of xanthoma or a terminal stage of erythema elevatum diutinum

Treatment is unnecessary spontaneous cure is reported to occur after months or years

NECROBIOSIS LIPOIDICA

Necrobiosis lipoidica (Oppenheim Urbach) is a relatively rare disease affecting adults women much oftener than men. Sufferers are frequently but not always, diabetics and the condition may be a forerunner of diabetes Urbach originally described it under the term necrobiosis lipoidica diabeticorum. Vascular changes appear to determine the disease in all cases whether diabetics or not In diabetics there is no apparent connection between the degree of severity of the diabetes and the skin eruption and control of the diabetes has no influence on the lesions In any case of necrobiosis lipoidica it is essential to check and recheck on the possibility of diabetes.

Lesions most frequently arise symmetrically on the shins suggesting that trauma may play some part in their precipitation, but any skin area may be affected The commonest variety is of atrophic sclerodermiform plaques, sometimes discrete sometimes coalescing to cover large areas with circinate or serpiginous edges The slightly-depressed firm centre is of chamois leather colour flecked sometimes with brown, with a thin atrophic epidermis scaling telangiectasia and erosions or ulcerations may occur The border zone is a little elevated infiltrated and red to violet in colour (Fig 258)

With ulcerative lesions the appearance of a syphilitic gumma may be almost exactly simulated In other cases the lesions may resemble those of typical or atypical granuloma annulare

erythema elevatum diutinum or gouty tophi, and histological examination is essential for accurate diagnosis.

Histopathology The epidermis is atrophic. Throughout the dermis are scattered areas of necrobiosis of collagen in which the degenerate collagen bundles are swollen, broken up and irregularly arranged. A cellular infiltrate of histiocytes,



FIG. 158
Necrobiosis lipoidica
[St Thomas' Hospital]

lymphocytes, fibroblasts and occasional epithelioid and giant cells is found, especially about the vessels, around the necrobiotic areas and, to a lesser extent, in them. The blood vessels show fibrosis of their walls, endothelial proliferation and, sometimes, occlusion of the lumen or thrombosis. Special staining frequently shows lipid droplets in the areas of necrobiosis their presence is presumably a secondary phenomenon. The picture is in many ways reminiscent of that of granuloma annulare and a relationship between the two conditions has been suggested

Treatment is ineffective. Excision and repair should be contemplated only when all activity appears to have ceased.

GRANULOMATOSIS DISCIFORMIS CHRONICA ET PROGRESSIVA (Miescher)

This condition is considered here because of its clinical and histological resemblance to necrobiosis lipoidica and because it is believed by many to be a variant or precursor of the latter The lesions may be found on the shins and are then atrophic and sclerodermiform On other sites they may take this form or that of granuloma annulare In three cases I have seen the lesions, all on the forehead or neck, were slowly-spreading rings, up to 5 cm diameter that merged into one another The borders were elevated firm ridges, 1 to 2 mm wide and showing faint beading reminiscent of that seen in granuloma annulare In another case the clinical appearances of porokeratosis Mibelli were reproduced

Histopathology Under an atrophic epidermis is an abundant dermal infiltrate densest in the upper region but reaching down to the level of the hypoderm which itself is unaffected The infiltrate consists of a variety of cells the most striking of which are numerous giant cells mostly of the foreign body type but also of the Langhans type These giant cells may be surrounded by lymphocytes and epithelioid cells, but the picture is seldom tuberculoid or they may be found at the borders of the infiltrate or alone and isolated between collagen bundles There are many histiocytes and some plasma cells Although the collagen fibres are disturbed and disrupted by this infiltrate there is no necrobiosis Vasculitis with endothelial proliferation and obliteration of the lumen is evident but the changes are not so marked as in necrobiosis lipoidica Special staining may reveal lipid droplets both within histiocytes and extracellularly but the quantity is never important

The status of granulomatosis disciformis is far from clear It may be a variant of necrobiosis lipoidica, but it has also been suggested that it may be a tuberculide or a manifestation of sarcoidosis Unlike necrobiosis lipoidica there is no frequent relationship to diabetes.

Treatment is ineffective

DISTURBANCES OF PHOSPHOLIPID METABOLISM

NIEMANN-PICK DISEASE (Lipoid histiocytosis)

This is a rare, rapidly fatal, hereditary (recessive) and familial disease of Jewish infants. Abnormal deposits of sphingomyelin are found in the reticulo-endothelial cells of many organs, but not in the skin.

The disease manifests itself in the early months of life with hepato-splenomegaly adenopathy a swollen abdomen, oedema, idiocy and wasting The skin has a greyish-brown colour due to increase of melanin. Amaurotic idiocy and retinitis pigmentosa may be associated.

GAUCHER'S DISEASE

In Gaucher's disease kerasin is deposited in the reticulo-endothelial cells of many organs, but not in the skin. Hyper pigmentation of the skin of a greyish-brown colour occurs especially on the exposed areas, in some cases and is due to increase of melanin.

The disease is hereditary (dominant) and familial and occurs most frequently in Jews, but all races may be affected. It may manifest itself at any age, but can be broadly divided into infantile and adult types.

The acute infantile type begins in the early months and ends in death after a year or two. The child deteriorates mentally and physically there is enlargement of the liver and spleen with swelling of the abdomen and a variety of nervous disorders including squint, muscular weakness and catatonia.

The adult type begins insidiously and runs a long downhill course. There is enlargment of the spleen, liver and lymph glands and decalcification and hypertrophy of the long bones. Leukopenia, thrombocytopenia and haemorrhages may occur Gaucher foam cells, whose kerasin content may be stained by the periodic acid-Schiff technique, are found in biopsy material from affected organs.

AMYLOIDOSIS

Amyloid is a complex substance composed of a protein fraction, derived from globulins, and a variable polysaccharide

fraction It is not known whether amyloid originates from local degeneration of tissue or is deposited as a result of plasma protein disturbance Amyloid is found in the skin and other organs in three rare conditions

Secondary systemic amyloidosis amyloid disease occurs with chronic infective diseases such as osteomyelitis, tuberculosis, leprosy and syphilis and with chronic cachectic diseases associated with marked protein loss Deposits of amyloid are found especially in the liver spleen kidneys and adrenal glands. *Only in exceptional cases is the integument involved*, but a diffuse hard infiltration of the skin and nodular lesions of the lips have been described

Primary systemic amyloidosis (Lubarsch Pick) differs from secondary amyloidosis in that the organs commonly affected in the latter are usually spared and the sites of election for the deposits are the smooth and striated muscles the small blood vessels the gastro-intestinal tract and the skin and mucous membranes Multiple myeloma is so frequently associated that it is questionable whether the use of primary in the title is justified A search for evidence of multiple myeloma is essential in all cases of apparently primary systemic amyloidosis. The disease occurs in adults, usually over forty years, and is eventually fatal

The possibility of deposition of amyloid in practically any organ allows a great variety of manners of presentation of the disease which if the skin be uninvolved (lesions are found in *only 20 per cent of cases*) may be recognized only at autopsy The disease may cause symptoms of cardiac insufficiency or failure symptoms referable to all levels of the gastro-intestinal tract or muscular weakness, pain or swelling to mention only a few of the possibilities

A variety of skin lesions may be found Disseminated eruptions of petechial or ecchymotic haemorrhages are due to invasion of the walls of small blood vessels.

Deposition of amyloid in the dermis may produce an eruption of little firm, translucent pink, yellowish or waxy papules or plaques of hard white or yellowish sclerodermiform infiltration Vesiculo-bullous lesions, nodules hyperpigmentation of the eyelids or of a more diffuse nature and an orange colouring of the skin are also described

Macroglossia is common and the tongue may be greatly enlarged and hard and its surface studded with nodules, bullae, fissures and furrows. The lips, cheeks, pharynx and larynx may be involved the nasal and ano-rectal mucous membranes are more rarely affected.

The course of systemic amyloidosis, whether associated with multiple myeloma or not, is towards death after 2 or 3 years.

No effective treatment has been discovered.

Primary cutaneous amyloidosis (Gutman Freudenthal) or lichenoid amyloidosis is a benign disease of adults. The lesions, which may appear after a phase of pruritus, are grouped papules or nodules, firm in consistency pink to brown in colour and smooth or verrucous on the surface they usually itch. Sites of election are the legs, the extensor surfaces of the arms and forearms and the back, but any area may be involved distribution is usually symmetrical. No organ apart from the skin is involved.

The lesions may resemble those of Darier's disease, colloid milium, lichen verrucosus or lichen simplex chronicus and diagnosis usually rests on histological examination.

Treatment is ineffective.

Congo-red tests are used in the investigation of amyloidosis. In the Paunz Benhold test 10 c.c. of a 1 per cent solution are injected intravenously In secondary systemic amyloidosis the dye disappears rapidly from the plasma, between 90 and 100 per cent having been eliminated in the first hour The test is negative (less than 40 per cent decolorization) in primary cutaneous amyloidosis and may be negative, doubtful or positive in primary systemic amyloidosis.

Subcutaneous (1 c.c.) or intradermal (0 1 c.c.) injection of Congo-red solution in affected areas produces selective staining of deposits of amyloid after 24 to 48 hours.

Histopathology Special staining techniques are required to identify amyloid. With Van Gieson's stain amyloid stains yellow-brown and collagen red. Congo-red, periodic acid-Schiff and Paris-violet also have an affinity for amyloid and a variety of stains may have to be employed in some cases because of the varying constitution of the complex.

In primary systemic amyloidosis the amyloid is found in large amorphous masses at all levels of the dermis and

hypoderm in the membrana propria of sweat glands, around blood vessels and in their walls. In the hypoderm, amyloid rings may be seen where the substance has been deposited around fat cells

In primary cutaneous amyloidosis the amyloid deposits are smaller and occur mainly in the subepidermal zone. A mild lymphocytic infiltrate may be found

MYXOEDEMA

There are three distinct types of myxoedema, but in all of them there occurs a deposition of mucin in the skin Generalized myxoedema is associated with hypothyroidism, circumscribed myxoedema with hyperthyroidism, and papular myxoedema occurs in the absence of any thyroid disturbance.

The staining properties of mucin indicate that it is a protein polysaccharide complex and that it contains a large amount of hyaluronic acid Mucin stains light blue with haematoxylin and eosin red with periodic acid-Schiff and is strongly metachromatic with methylene blue it is digested by hyaluronidase.

Generalized myxoedema This is the classical variety of myxoedema the result of hypothyroidism. The disease in full development is often recognizable in the face alone. The face is swollen the nose enlarged the lips thickened and the eyelids bloated the skin is generally yellowish with reddish-blue tones at the cheeks and the whole aspect is cretinous (Fig 259) The skin as a whole is slightly infiltrated and seems oedematous but there is no pitting on pressure it is dry cold and waxy The hands and feet are swollen the nails dry furrowed and fragile the hair sparse and the tongue swollen Life both mental and physical is at a low ebb

Mucin is demonstrable in small quantity between the collagen fibres and bundles in the oedematous dermis. The diagnosis is usually established without the aid of biopsy and treatment with thyroid extract is most effective

Circumscribed myxoedema is found usually associated with exophthalmos as a manifestation or a precursor of hyperthyroidism it may follow thyroidectomy or treatment with thiouracil. The lesions, commonly bilateral are found on the

skins (pretibial myxoedema) as firm swollen, non-pitting round or oval plaques with a smooth or papular surface. The epidermis is stretched, yellowish or brownish in colour and the follicular orifices are prominent.

Large deposits of mucin are found in the dermis, especially in the lower reaches, together with fibroblasts (some stellate) and a mild perivascular infiltrate. The collagen fibres are separated and the elastic fibres decreased in quantity

Treatment of the thyrotoxicosis may improve the skin condition. Local injections of hyaluronidase are reputed sometimes to have been effective.



FIG. 259
Myxoedema.

Papular myxoedema, papular mucinosis, is seemingly unassociated with any thyroid abnormality The lesions are discrete or aggregated waxy papules, little plaques or rings. In some cases large plaques with peripheral papules are found and verrucous lesions may develop especially about the ankles and legs. Distribution is symmetrical with the extensor surfaces of the limbs and the face, which may become swollen and leonine, as sites of election.

The histological picture is like that seen in circumscribed myxoedema. In some cases a variety of staining techniques

must be employed to distinguish the mucin deposits from those seen in amyloidosis or colloid milium.

Treatment is ineffective

CALCINOSIS CUTIS

Metastatic calcification results from hypercalcaemia which may be due to parathyroid tumours, excessive intake of vitamin D chronic renal disease or destructive bone diseases such as osteomyelitis or malignant tumours. Deposition of calcium takes place usually in the kidneys, lungs and stomach and only very rarely in the skin or subcutaneous tissue.

Metabolic calcification is relatively common and occurs in the absence of hypercalcaemia as a result presumably of local metabolic disturbances. Calcium may be deposited in the skin and subcutaneous tissues or sometimes, in the muscles and tendons but the internal organs are spared Calcinosis circumscripta or universalis are descriptive terms used respectively for localized and disseminated lesions

Calcinosis cutis may be suspected clinically from the consistence of lesions or discharge of their contents or discovered only on radiological examination Calcareous deposits are fairly common in scleroderma and dermatomyositis. They may also be found in tumours such as epidermal cysts, fibromas and the calcifying epithelioma of Malherbe. They may occur in scars of all kinds even in acne scars and in the hypoderm after any panniculitis.

The stony tumours of Poirier are little gritty nodules on the inner sides of the shins in elderly people they appear in the line of veins.

Calcinosis universalis, or calcareous gout is characterized by stony hard and radiopaque nodules especially near the finger joints, but also near the large joints or elsewhere on the skin They are red and painful at first later indolent and may ulcerate and discharge their gritty contents of calcium phosphate and carbonate through fistulae that are very slow to heal The condition may occur at any age and there may be a great many lesions. Calcinosis universalis occurs most commonly with scleroderma (Thibierge Weissenbach syndrome) and

dermatomyositis and has also been described in association with Raynaud's disease, poikiloderma and acrodermatitis chronica atrophicans, but in many cases no cause is discovered.

Histopathology Calcium deposits in the skin stain deep blue with haematoxylin and eosin, black with von Kossa's stain. A granulomatous reaction with foreign-body giant cells is commonly found around the deposits.

GOUT

Gout is a disturbance of purine metabolism characterized by recurrent attacks of arthritis and sometimes by nodular skin lesions known as tophi. Gouty tophi are formed by the deposition of urates in the dermis and hypoderm and are found on the margins of the helix of the ear at the distal interphalangeal joints of the fingers and, more rarely near the elbows or knees or elsewhere. In its earliest days a tophus is a painful inflammatory swelling which may disappear entirely but which usually subsides only partially to leave a hard nodule. The urate deposit shows white through a normal or violaceous skin. Subsequent attacks of gout may bring enlargement of the original nodules and the appearance of fresh nodules around them. Ulceration and the discharge of a chalky substance may occur

Histopathology The tophus consists of sheaves of needle shaped urate crystals surrounded by granulation tissue containing many foreign-body giant cells.

Treatment of the gout, however well it may act on the arthritis, usually has little effect on chronic tophi which must be surgically removed when they are inaesthetic or hindersome.

DIABETES

A great variety of skin lesions may appear in the course of diabetes or as a result of its treatment. Such lesions are not specific for the disease, but some of them may be of diagnostic significance.

The following are lesions that may prompt an investigation for diabetes. Generalized pruritus may rarely be the first sign of diabetes itching soon disappears on treatment but may recur

must be employed to distinguish the mucin deposits from those seen in amyloidosis or colloid milium

Treatment is ineffective.

CALCINOSIS CUTIS

Metastatic calcification results from hypercalcaemia which may be due to parathyroid tumours, excessive intake of vitamin D chronic renal disease or destructive bone diseases such as *osteomyelitis or malignant tumours* Deposition of calcium takes place usually in the kidneys lungs and stomach and only very rarely in the skin or subcutaneous tissue.

Metabolic calcification is relatively common and occurs in the absence of hypercalcaemia as a result presumably of local metabolic disturbances Calcium may be deposited in the skin and subcutaneous tissues or sometimes in the muscles and tendons but the internal organs are spared Calcinosis circumscripta or universalis are descriptive terms used respectively for localized and disseminated lesions

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to avoid infection by the routine use of an antifungous powder Corns and calloses should equally be carefully tended so as to avoid secondary infections.

Gangrene is the most dangerous complication of diabetes and results from vascular sclerosis. It may start spontaneously but usually follows trauma or infection in the skin. The feet and legs are oftenest affected, but any skin area and even mucous membranes may suffer

Rarer complications such as hyperhidrosis and hypohidrosis are mainly of academic interest. Diabetes is often associated with lipoid proteinosis and, according to some authors, with Kaposi's acrosarcomatosis. Benign acanthosis nigricans is also noted as having occurred in diabetics, presumably obese patients

Complications of treatment. Signs of avitaminosis as a result of dietetic restrictions have been described and carotin pigmentation may occur

The modern insulins cause few complications but some patients develop local reactions of erythema and swelling at injection sites in the first weeks of treatment such reactions disappear spontaneously

Insulin lipodystrophy is common this is a local fat atrophy at injection sites and the skin becomes atrophic and sunken. Local hypertrophy of subcutaneous fat occurs occasionally These phenomena are the result of interference with metabolism of fat. Some patients on insulin develop a slight oedema of the face with a yellowish or waxy tint in the skin.

Allergic reactions of erythematous urticarial or even purpuric type occur rarely with any type of insulin. Sometimes one particular brand is not tolerated and a change to another relieves the symptoms.

Insulin is usually manufactured from pork and beef pancreas pure beef insulin is available for patients sensitive to the mixture The very rare cases sensitive to any type of insulin must be rapidly desensitized by frequently repeated injections of small but increasing doses

Allergic reactions to the latest antidiabetic drugs such as carbutamide and tolbutamide are fairly common. These substances are related to the sulphonamides and cause the same types of reactions in the skin and other organs.

if the disease gets out of control Patients with hypoglycaemia may also itch

Diabetics are more than normally liable to develop coccal or fungous infections of the skin It is standard practice to check for diabetes in cases of furunculosis and carbuncles but the number of diabetics so discovered is very small

Infective eczema of the vulva and thighs is often the first manifestation of diabetes in women and it is essential to test the urine in all cases of pruritus vulvae. The eczema may be dry and scaling or moist and vesicular and always itches severely This is not an allergic reaction to sugar in the skin or urine but a coccal or monilial infection the sugar serving as an admirable culture medium for the microbes Control of the *diabetes usually brings speedy relief but local treatment with* antibiotic ointments (e g aureomycin nystatin) may be required A similar itchy eczematous balanitis, starting usually around the meatus, is seen in men

Diabetes (severe with lipaemia) is sometimes discovered to be the cause of xanthomatosis The disseminated rash of yellow papules and nodules appears suddenly and new lesions erupt in crops any area of the skin may be affected Some lesions show an inflammatory halo and pustulation and ulceration may occur itch may be severe Diet and insulin are usually curative

Necrobiosis lipoidica is frequently associated with diabetes and may appear months or years before other signs of the disease are manifest The lesions are usually unaffected by insulin therapy

The above lesions may equally arise in the course of diabetes. Those that follow may complicate diabetes but are not of diagnostic importance Coccal infections of all kinds are common in diabetes, but are usually controlled by antibiotics with severe infections the dosage of insulin may temporarily have to be increased Moniliasis of the skin and mucous surfaces, apart from the vulvitis already noted is commoner on the diabetic than on the normal skin but generally reacts to locally applied nystatin

Fungous infections of the feet are common and must be treated with care because of the possibility of their leading to gangrene. Susceptible subjects should take the greatest care

tion of the families of patients discloses sufferers from the disease in latent form. Hepatic porphyria commonly manifests itself in adult life between 16 and 50 years, although children may be affected. Acute porphyria occurs oftener in women than in men, but the taint is equally distributed between the sexes in affected families. There are also variations in the types of porphyrins excreted, but these are not yet sufficiently clearly understood to serve as a basis for classification.

The hepatic porphyria common in Sweden is clearly different from that found among the white and the Bantu inhabitants of South Africa. Many Swedish cases trace their ancestry back to a common ancestor. The symptoms are always those of acute porphyria, often precipitated by the use of drugs, commonly barbiturates. In no case have skin lesions been discovered. There is a marked increase in excretion of porphobilinogen and of amino-laevulinic acid during acute attacks and for long afterwards. porphyrin excretion is little increased except during attacks.

The hepatic porphyria of white South Africans is also a familial disease, and the first sufferer was a Hollander who settled early in the eighteenth century. Active or scarred skin lesions are found in most cases, but patients, particularly women, may also suffer from attacks of acute porphyria which are usually precipitated by the use of drugs, commonly barbiturates. Porphobilinogen excretion is increased in acute attacks, but soon reverts to normal if the patient recovers. Excretion of urinary and faecal porphyrins is greatly increased in acute attacks, but abnormal quantities are often found in the urine and oftener still in the faeces between attacks. Porphyrin excretion is also increased in patients with chronic cutaneous porphyria and in those relatives of sufferers who bear the taint in latent form. South African porphyria is basically chronic cutaneous porphyria, and acute episodes probably occur only after provocation, as by the use of certain drugs. A latent porphyric may be provoked to an acute attack before skin lesions have developed, and the clinical picture though not the biochemical, then copies that of the Swedish porphyria.

Porphyria in the pure Bantu population of South Africa is also of the chronic cutaneous type like that seen in the Caucasians, but distinguishing features are the rarity of acute

THE PORPHYRIAS

The porphyrias are disease syndromes associated with disturbances of pyrrole pigment metabolism and characterized by the continuous or intermittent excretion of abnormal quantities of porphyrins in the urine and faeces The syndromes with which we are chiefly concerned occur in persons suffering from inherited defects and not in those where increased porphyrin excretion is only secondary to some other disease or intoxication

The porphyrias are divisible into two main categories erythropoietic porphyria, of which congenital porphyria is the only example, and hepatic or familial porphyria of which there are several variants In erythropoietic porphyria the porphyrins are concentrated mainly in the bone marrow and the trait is recessive In hepatic porphyria the porphyrins are concentrated in the liver and the mode of inheritance is in dominance

Erythropoietic porphyria

Congenital porphyria is a very rare condition and only a score or so of genuine cases have been reported Signs of disease are evident in early infancy and include the passage of dark or red urine severe photosensitivity with bullous eruptions on exposed skin leading to scars and even mutilations, hyperpigmentation of exposed and unexposed skin hypertrichosis, anaemia and splenomegaly The milk teeth are pink and fluoresce under Wood's light and the bones may equally be stained with porphyrins Treatment is unavailing and such patients often die of tuberculosis at an early age

Hepatic porphyria

Hepatic porphyria is found all over the world and in all races but it is especially common in Sweden and South Africa where it has received particular study There are both clinical and biochemical variants of hepatic porphyria. The clinical variants are acute porphyria characterized by acute abdominal and neurological symptoms and chronic cutaneous porphyria (porphyria cutanea tarda) with skin lesions of which bullous eruptions on exposed areas are the most important Investiga-

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It sometimes appears as if bullous lesions are the result of photosensitivity (hydroa aestivale porphyricum) but it is always difficult to exclude the possibility of trauma and protection against sunlight, as by the use of chloroquine is rarely beneficial. The bullous lesions rupture and, if no secondary infection is incurred, the resulting excoriations heal in a week or two. Depigmented or pigmented scars may be left and these



FIG. 260

Chronic cutaneous porphyria. Note hyperkeratosis over knuckles on right.

are sometimes valuable clues to diagnosis in inactive cases or in cases of suspected acute porphyria (Fig 260) Scarring is occasionally so severe as to cause mutilation and deformity of the hands or face such cases have been misdiagnosed as lepers. Milia may form in scars and nails may be loosened or deformed by subungual bullae. A labouring man with chronic porphyria is often entirely incapacitated.

Sometimes no bullae form, but the exposed skin is more tender than normal, easily scraped off and unusually liable to

attacks and less markedly abnormal excretion of porphyrins in the faeces of sufferers The mode of inheritance of porphyria in the Bantu is not yet clear as their complicated family ties make investigation difficult.

Acute porphyria occurs oftenest in women and an attack is frequently provoked by the use of drugs. The barbiturates are the commonest offenders, but sulphonamides and rarely, chloroquine derivatives have been implicated The porphyric may be neurotic and given to complaining of vague disorders she will eventually be given a barbiturate and the acute attack is precipitated Symptoms are often aggravated by pregnancy Abdominal or nervous symptoms may predominate but both are usually present. Abdominal pains of varying severity may simulate anything between appendicitis and acute intestinal obstruction Constipation is the rule and vomiting is common. An operation at this stage particularly if thiopentone anaesthesia is used is often fatal

At the beginning of an attack the patient is often hysterical later she becomes lethargic or comatose Muscular weakness and paresis as a result of peripheral neuritis may go on to paralysis and death from respiratory failure Recovery of muscular function may take months

The fresh urine may be relatively normal in colour but it is usually red or dark and always darkens after standing for a few hours it contains an excess of porphobilinogen and porphyrins The presence of porphobilinogen is characteristic of acute porphyria it is not excreted in chronic cutaneous porphyria

Chronic cutaneous porphyria porphyria cutanea tarda, has three cardinal signs, *skin eruptions hypertrichosis and hyper pigmentation* all three are found in the classical case Signs of disease appear almost always in adult life but young children may be affected Men are affected oftener than women a finding opposite to that in acute porphyria

The commonest finding is an abnormal fragility of the skin, especially of the exposed areas with the appearance of serous or haemorrhagic subepidermal bullae on the hands and fingers and rather less often on the feet face arms, legs and friction points elsewhere as a result of relatively minor trauma. This phenomenon is known as epidermolysis bullosa porphyrica



FIG. 26

Chronic cutaneous porphyria. Erosions and scars on hand, hyperpigmentation of face.



FIG. 26a

Chronic cutaneous porphyria. Hyperpigmentation and hypertrichosis of face, impetiginized bullous eruption of hands.

minor coccal infections suggestive scarring, especially of the backs of the hands may be found in quiescent cases.

An *erythematous and vesiculo-oedematous dermatitis of* the exposed skin reminiscent of pellagra is said to occur It should be noted that *pellagra is not a cause of porphyrinuria*

I have noted that Bantu patients with chronic porphyria often show a velvety finely *verrucous hyperkeratosis of the* two terminal finger knuckles Sclerodermiform thickening or lichenification of the skin of the face neck and upper chest with epidermal atrophy and pigmentary changes may also occur

Hyperpigmentation of the exposed skin, especially of the cheeks and temples, is common and most marked in the dark skinned races where the colour may vary from chocolate to jet black rarely larger areas or the whole body surface may darken Pellagrous pigmentation may closely be simulated Hyperpigmentation may be a solitary sign of porphyria and is, in South Africa, quite often the reason why a patient seeks attention

Hypertrichosis frequently accompanies hyperpigmentation but it may be found on a normal-coloured skin It is easily recognized in women The triangular areas between the outer ends of the eyebrows and the temporal hair are oftenest affected, the cheeks nearly as often and the upper lip arms and legs less frequently (Figs. 261 and 262)

Ocular conjunctival lesions analogous to the bullous lesions on the skin may occur Acute oedematous and chronic pigmentary lesions of the fundus may be discovered especially in patients who have suffered acute attacks

The state of sensitivity of the skin in chronic porphyria varies greatly in intensity For months at a time bullae may form at the least provocation and then for a spell the skin may be relatively normal Once started attacks persist indefinitely though there is a definite tendency to spontaneous permanent recovery after the age of fifty Although the disease may produce minor or major disability because of lesions on the hands it has, in those who escape attacks of acute porphyria, no grave prognostic significance. Chronic porphyrics, in South Africa at least, are not often of high intelligence They are apt to be rather backward and both mentally and physically constipated.



FIG. 260

Chronic cutaneous porphyria. Erosions and scars on hand, hyperpigmentation of face



FIG. 261

Chronic cutaneous porphyria. Hyperpigmentation and hypertrichosis of face, depigmented bullous eruption of hands.

The excretion of urinary porphyrins varies greatly a is not always directly related to the state of sensitivity of t skin. When chronic cutaneous porphyria is suspected a sing negative test should not lower the index of suspicion At tim there may be a normal excretion of porphyrins even when acti bullae are present.

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An even simpler test not quite so searching for excess o porphyrins in urine or faeces (a tiny quantity can be obtained from the rectum on the gloved finger) is to examine with Wood s light specimens shaken up with a mixture containing equal parts of amyl alcohol ether and glacial acetic acid a pink fluorescence indicates a positive result.

Porphobilinogen is present only during acute attacks in patients with chronic cutaneous porphyria The urine darkens on standing The Watson-Schwartz test is used for precise identification

The bullae of epidermolysis bullosa porphyrica are sub-epidermal but there are no specific histological changes helpful in diagnosis

Treatment There is no specific treatment for any variety of porphyria The patient with chronic cutaneous porphyria learns to protect himself to some extent but in cases with very marked fragility of the skin a change of occupation may be necessary Only very rarely is exposure to sunlight a major factor in the cause of bullae I have freque[illegible]cribed Mepacrine o[illegible] compounds, but [illegible] occasions h[illegible] seemed to redu[illegible] to bulla fo[illegible] s of acute porphy[illegible] reported foll[illegible] drugs.

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